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ABSTRACTS

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## CLINICAL STUDIES, TUBERCULOSIS

**Childhood Tuberculosis.**—The tuberculosis mortality figures of Sheffield children for the last thirty years show that the number of annual deaths did not fall between 1934 and 1947. After that, the death rate dropped fourteen fold in five years, from 25 in 1947 to 1.8 per 100,000 in 1952. This decline of tuberculosis mortality in children far exceeded that in adults and the decline of mortality in children from all other causes. In Great Britain as a whole, the fall was considerable during the same period but was less than fivefold except in Sheffield. Successful treatment with streptomycin of otherwise fatal tuberculosis in children was responsible for this improvement up to and including 1949. Since 1950, preventive measures, namely, intensified contact examinations, segregation, and BCG vaccination of children in tuberculous families and households, may have been as important as streptomycin treatment in the progressive reduction in mortality. This has been the work of a tuberculosis contact clinic for small children. Increasing effort and vigilance should further reduce tuberculosis morbidity. The fundamental methods of tuberculosis control, assisted by BCG vaccination and effective chemotherapy, should quickly eliminate deaths from this cause in children.—*The mortality from childhood tuberculosis in Sheffield, J. Lorber, Brit. M. J., November 21, 1953, No. 4846: 1122.*—(*E. A. Riley*)

**Diagnosis of Childhood Tuberculosis.**—Chronic nontuberculous infections of the lungs may simulate primary tuberculosis, and nonpathogenic acid-fast bacilli may be ingested with food and drink. Hence, isolation of acid-fast bacilli from the gastric contents of a tuberculin-negative child does not prove tuberculosis unless the organism is pathogenic. Not all acid-fast bacilli found in the sputum are from the lung, and in one case the nasal discharge was the source of acid-fast bacilli in the sputum. With few exceptions, a persistent negative tuberculin reaction is strong evidence against active tuberculosis. To avoid the risk of exposing a child to tuberculosis, no undiagnosed case should be admitted to a tuberculosis hospital.—*Some problems in the diagnosis and treatment of pulmonary tuberculosis in childhood, H. Hsu & J. T. Szypulski, J. Pediat., December, 1953, 43: 661.*—(*M. J. Small*)

**Tuberculosis Conference of the Russian Academy of Medicine.**—A Conference of the Russian Academy of Medicine on the problems of tuberculosis, held at Yalta, in October, 1952, was attended by 600 persons. The influence of the nervous system on the pathogenesis of tuberculosis in the light of Pavlov's teaching was one of the chief subjects of discussion. *Lebedeva*, director of the Tuberculosis Institute of the Academy of Medicine, concluded from observations on human material that the isolated tuberculous lesions in lungs, kidneys, and joints are related one to another. Animal experiments have showed that the tuberculous lesions develop in different organs and tissues at the same time and have revealed the groundlessness of the old teaching of a primary complex in tuberculous infection. *Tchernigovsky* and *Kan* reported that the sensitivity of different organs to tuberculous infection is directly related to the innervation

of the tissue. The resistance to tuberculosis of the lungs can be increased or decreased by intervention of the vagus nerve. The innervation of the lungs depends on the defense functions of the higher parts of the nervous system. *Miasnikow* indicated that cutting the nerves is a crude experiment and cannot explain the mechanism of the pathogenesis of tuberculosis. *Mikeladze* and *Sharashidze* studied the pathologic changes in the nervous system of the genital organs during tuberculosis. *Kharkow* investigated the delaying and stimulating functions of the central nervous system on tuberculosis by means of bromine and caffeine. *Semenow*, director of the Tuberculosis Institute of Læningrad, characterized the function of the higher parts of the nervous system in tuberculosis infection. By means of chronaximetry, plethismography, and by investigating the reflex regulation of stomach secretion, he discovered a connection between the function of the higher parts of the nervous system and the course of the tuberculous process. A considerable number of the reports were dedicated to the problem of tuberculosis as a general disease of the organism. *Schmelev*, discussing the primary forms of tuberculosis, indicated the necessity for treating primary tuberculosis as a disease of the whole organism. —*Scientific Meeting of the Section of the Academy of Medicine of Soviet Union on the Problems of Tuberculosis* (*Russian*). *Problemi Tuberkuloza, March–April, 1953, No. 2, 74.*—(*E. Darzins*)

**Vascularization of Tuberculous Cavities.**—Most angiocardiographic studies of tuberculous cavities *in vivo* indicate that they are excluded from the pulmonary circulation and present an impermeable barrier to therapeutic agents. On the other hand, histologic examination always reveals numerous vessels in the cavity wall, particularly certain thick-walled arteries with narrow lumens. They have a thin layer of peripheral, circular, contractile fibers and a thick inner layer of longitudinal muscle fibers; the latter consist of pale cells forming a series of transitions between the muscular fusiform and the typical epithelioid form. The endothelium shows cubic metaplasia. Autopsy and surgical specimens of lungs containing cavities or tuberculomas with a minimum diameter of 5 cm. were studied by injecting the bronchial and pulmonary arteries with a mixture of gelatine and lead oxide, by anatomical roentgenography, and histologic examination. Injection of the specimens *via* the pulmonary arteries revealed that the injected material penetrated into the wall of the cavity through small, sinuous vessels radiographically typical of bronchial arteries. Examination of 2,500 serial sections showed that the bronchial arteries or their collaterals meet the obliterated pulmonary arteries, in the vicinity of the bronchial pedicle. Where the bronchial arteries join the pulmonary arteries the latter have a break in the continuity of their elastic membrane. The bronchial arteries penetrate the obliterated part of the pulmonary arteries to reach the nonobliterated portion and to enter the cavity wall where they form many small dilated vessels within the granulation tissue. These anastomotic arteries are surrounded by arterioles which are also modified. Thus, the cavity wall is supplied by new anastomoses between bronchial and pulmonary arteries which are rarely present in the normal lung. Tuberculomas, injected in the same manner, also showed anastomoses between bronchial and pulmonary arteries, more numerous than in the normal lung but much less developed than around cavitary lesions. In 4,500 sections of tuberculomas, radiographic examination showed that most of the pulmonary arteries were not obliterated. In a few places only pulmonary arteries were obliterated and re-canalized by bronchial arteries; it was precisely in these areas that the caseum showed softening and liquefaction. Thus, vascular modifications around and within tuberculous foci determine not only the pathogenesis but the future development of these foci, particularly the liquefaction and solidification of caseous material.—*Étude comparée de la vascularization des cavernes tuberculeuses et des foyers caséeux circonscrits, rôle du régime circulatoire dans la liquéfaction*

*du caséum, J. Delarue, C. Sors, & J. Mignot, Rev. de la tuberc., 1953, 17: 609.—(V. Leites)*

**Electroencephalograms in Tuberculous Meningitis.**—A series of 408 electroencephalographic tracings taken at monthly intervals during the entire course of 59 children with tuberculous meningitis usually showed tracings, slow peaks, and rapid rhythms of high voltage. The electrical anomalies frequently were most marked in posterior areas, but this localization had no prognostic significance. The tracings were often asymmetrical, usually without clinical localization. The prognostic value of the initial tracing was great: in 75 per cent of the fatal cases, the initial tracing was much altered; among the curable cases, the first tracing showed marked alteration in only 35 per cent. An abnormal initial tracing had greater prognostic significance than did disturbed consciousness. As a rule, electroencephalographic findings paralleled the clinical course, electrical improvement usually following soon after the clinical improvement. Slight anomalies persisted in half of the cases long after clinical cure and the end of treatment but finally disappeared in most instances. It is difficult to infer the topography of lesions from the morphology and localization of the electrical changes (Authors' summary).—*Étude de l'électroencéphalogramme dans la méningite tuberculeuse de l'enfant Valeur pronostique, P. Laget, Ch. Bach, C. Alufi, & R.-A. Marquezy, Presse méd., July, 1953, 61: 984.—(V. Leites)*

**Atypical Course of Renal Tuberculosis.**—The clinical symptoms of renal tuberculosis are quite variable. A case with an atypical course may be difficult to recognize as tuberculosis of the kidney. Two patients with the pseudolithic form of renal tuberculosis (Tuffier) were under treatment for osteopathic forms of tuberculosis and, therefore, in spite of atypical clinical manifestations and negative bacteriologic tests, diagnosis was not difficult. Repeated renal colic was probably due to irritation by the eliminated caseous material. Urogenital tuberculosis is third in frequency among extrapulmonary tuberculous processes. Diagnostic errors are frequent and occur most often in the course of the pseudolithiatic form of renal tuberculosis. False diagnoses of nephrolithiasis, appendicitis, hydronephrosis, contusion, and low back pain are frequent, and the tuberculous character of the illness may remain unrecognized for a long time.—*Contribution to the diagnostics of atypical course of kidney tuberculosis (Czech), J. Coufal, Lék. listy, November 1, 1953, 8: 489.—(J. Ilavsky)*

**Renal Tuberculosis.**—Results of bacteriologic studies of 3 small tuberculous lesions of the kidney removed after prolonged preoperative chemotherapy were positive in respect to acid-fast bacilli but were negative in so far as both culture and inoculation of guinea pigs were concerned. In contrast, other tuberculous kidneys removed because of larger lesions or after short periods of preoperative chemotherapy were found to contain viable bacilli which produced tuberculosis in guinea pigs. Until the clinical significance of the apparent sterility of the small lesions is known, nephrectomy or heminephrectomy seems advisable for such lesions when the other kidney is free of roentgenographically demonstrable disease (Authors' summary).—*Bacteriological studies of tuberculous kidneys, S. E. Sivertson, L. A. Weed, & D. T. Carr, Proc. Staff Meet., Mayo Clin., October 7, 1953, 28: 554.—(E. A. Riley)*

**Bilateral Epididymal Tuberculosis in a Child.**—Bilateral tuberculous epididymitis in a 2-year-old child was treated by epididymectomy and removal of sinus tracts. There was no clinical evidence of tuberculous involvement of the prostate, seminal vesicles, or kidneys. Hematogenous spread to the epididymis from a primary pulmonary tuberculous infection was probable. The child had a proved tuberculous contact in his home.—*Bilateral epididymal tuberculosis in an infant, C. A. Wattenberg, M. Abrams, H. K. Lewis, & J. Lewis, J. Pediat., October, 1953, 43: 443.—(M. J. Small)*

**Skeletal Tuberculosis.**—A series of 156 cases of bone and/or joint tuberculosis followed in the Bronx Veterans Administration Hospital in the last ten years included some patients with unusual roentgenographic manifestations. Of the 156 patients, 95 had lesions in the axial skeleton, 13 in the ribs, and 68 in the peripheral bones. The unusual forms of spinal disease included lytic, productive, and proliferative types. The incidence of productive changes in the dorsal and lumbar vertebrae was 18 per cent. Sacro-iliac disease was unusually frequent, there being 24 cases. Roentgenographically detectable hematogenous dissemination to the skeletal system was also relatively common. Of the entire series, 56 patients had associated active, chronic pulmonary or renal lesions. In 34 cases (approximately 20 per cent) the bone lesion was associated with an active pulmonary disease; in 33 there was coexistent tuberculosis of the genitourinary system. In 8 patients, there was associated skeletal, renal, and pulmonary tuberculosis.—*Skeletal tuberculosis, M. H. Poppel, L. R. Lawrence, & J. F. Jacobson, Am. J. Roentgenol., December, 1953, 70: 936.*—(*T. H. Noehren*)

**Costal Tuberculosis.**—Tuberculous osteomyelitis of the ribs comprises approximately 5 per cent of all cases of bone and joint tuberculosis. It is the most common inflammatory process involving the ribs, apparently being more frequent than all other causes combined. As in other forms of bone tuberculosis, the disease of the ribs is almost purely destructive and is second only to metastatic malignancy among destructive costal lesions. Local pain and a soft tissue mass, a "cold abscess", are quite common; a draining sinus may arise from the mass. The roentgenographic appearance is variable, depending upon the location of the rib lesion and the degree and the stage of its development. Differentiation from other causes of rib destruction sometimes is difficult, particularly from other infections and solitary osteolytic rib metastases. Needle biopsy may provide the diagnosis in obscure cases. The treatment of choice is resection, combined with streptomycin, provided there is no active pulmonary, vertebral, or systemic tuberculosis. A total of 23 cases of rib tuberculosis proved by biopsy, autopsy findings, or bacteriologic methods were seen at the hospitals of the Detroit Department of Health during 1938 to 1948 inclusive.—*Tuberculosis of the ribs, M. Tatelman & E. J. P. Drouillard, Am. J. Roentgenol., December, 1953, 70: 923.*—(*T. H. Noehren*)

**Tuberculous Cervical Lymphadenitis.**—The pathology of the surrounding tissues was studied in 200 cases of surgically treated tuberculous cervical lymphadenitis. There were only 5 cases where the submaxillary gland was involved. The process propagated more frequently along the fascial planes and in the interstitial connective tissue of the muscles but the muscle fibers were seldom affected. Extensive suppuration of the muscles was encountered, however, in elderly persons whose resistance was diminished and when senile involution of the lymphatics may have been a factor in the spread of the process. Subcutaneous fat tissue offers very little resistance to the progression of the cold abscess making its way toward the surface from the perforated lymph node. Ulceration of the overlying skin is followed by the formation of a sinus, and at this point secondary pyogenic infection sets in, which favors further softening. The tuberculosis colliquativa cutis is characterized by caseation, by productive lesions, and by proliferative changes in the epithelial layers which may assume the character of a papilloma. Deposits of calcium in the subcutaneous tuberculous tissue may originate from the underlying lymph nodes or may develop locally as a result of caseation. When the process persists for a long time with an open sinus, the tuberculous lesions may become predominantly productive and, in this case, the differential diagnosis from lupus may be very difficult. Healing is hampered by the proliferating epidermis, by the secondary inflammatory changes, and by the presence of calcifications. The chronic irritation and the possible persistence of viable tubercle bacilli

within the calcifications may give rise to lupus three or four years after the beginning of the process. The best prevention of lupus is removal of the tuberculous lymph nodes associated with chemotherapy and antibiotics. In the experience of the author, antimicrobial therapy alone is insufficient to treat tuberculous lymphadenitis, but it is a useful adjunct to surgical treatment.—*Die Erkrankungen der Weichteile und der Haut bei der Halslymphknotentuberkulose, G. Hasche-Klünder, Deutsche med. Wchnschr., February 6, 1953,* **6:** *199.*—*(L. Molnar)*

**Diagnostic Lymph Node Aspiration.**—Aspiration may replace biopsy or may be used with it to diagnose enlarged lymph nodes. The aspiration is made with a 6-to-8 cm. long, 18-gauge needle and the aspirated material is spread on slides which are stained with the Ziehl-Nielsen or Pappenheim method. If solid particles are extracted, sections may be made. The aspirate may also be cultured or inoculated in guinea pigs. No anesthesia is required and, if correctly done, there are no serious inconveniences. Diagnostic aspiration was performed in 150 children with enlarged cervical lymph nodes. In 15 of these, aged five to fifteen years, the lymph node tuberculosis was the only manifestation of the disease. Cytologically these cases were characterized by specific proliferation, and rare tubercle bacilli were found after a long search. In the second group, there were 116 children from one to four years of age with enlarged caseous lymph nodes as well as signs of disseminated hematogenous tuberculosis. Histologically, these cases had marked necrosis, and tubercle bacilli were easily found in more than half of them. In the third group there were 19 children of various ages whose lymph node tuberculosis was accompanied by pulmonary infiltration or benign pulmonary tuberculosis. Histologically, there was hyperplasia of the reticulum and of the lymphoid tissue. No tubercle bacilli were found in these cases.—*La puncion ganglionar en la tuberculosis infantil, F. E. Santa Maria, Rev. españ. de tuberc., March, 1953, no. 216: 111.*—*(L. Molnar)*

**Diagnostic Aspiration of Tuberculous Nodes.**—It is easier and simpler to aspirate lymph nodes than to biopsy them for diagnostic purposes. Aspiration provides specimens for the differential diagnosis of simple inflammation, specific tuberculous inflammation, disease of blood forming organs and neoplasma. The specimens are stained by the Giemsa method. The cells of normal lymphatic nodules consist of prolymphocytes or immature lymphocytes. They constitute 60 to 70 per cent of the cells and are larger than mature lymphocytes. There are 25 to 30 per cent normal lymphocytes and 0.1 to 2 per cent basophilic and plasma cells. Among 242 cases of lymphadenitis, 102 specimens were of tuberculous, the rest of nontuberculous, origin. A specific cytologic picture of tuberculous lymphadenitis appears one to one and one-half months after the onset of infection. In 5 aspirated tuberculous fluids, a bloody aspect, the absence of specific tuberculous elements, and the predominance of prolymphocytes indicated an initial tuberculous process. As the disease progressed, the aspirated material contained specific elements of tuberculous tissue, such as epithelioid and giant cells. Epithelioid cells were agglomerated in considerable masses; sometimes they occupied a large part of the field of the microscope. The nuclei of epithelioid cells were oblong and about twice as large as those of monocytes. Epithelioid cells were discovered in 69.7 per cent and giant cells in 22.5 per cent of the cases of tuberculous lymphadenitis. When the caseous material was aspirated with a syringe, the stained films showed a granular mass without any structure. Among the granules and debris, some degenerated epithelioid and giant cells could be detected.—*The differential diagnosis of tuberculous lymphadenitis by means of puncture (Russian), E. D. Timasheva, Problemi Tuberkuloza, March–April, 1953, No. 2: 52.*—*(E. Darzins)*

**Segmental Resection or Collapse Therapy.**—Among 600 excisions for tuberculosis since 1949, 40 segmental resections have been performed, 30 of them within the last year. There

were 4 bronchopleural fistulas, only one of them among the last 30 cases. There was one empyema due to exogenous infection which cleared readily. There were 2 postoperative hemorrhages and 3 incomplete re-expansions. One patient still discharges tubercle bacilli eighteen months after operation. Although 29 patients show excellent early results, they have not been followed long enough for the late results to be apparent. More time must elapse before segmental resection can be compared with extrapleural pneumothorax, with which results have been most satisfactory. Among the last 1,000 of the latter, there was one operative death; 664 of the lesions would now be considered appropriate for segmental resection and among these patients there have been 2 late deaths and 90 per cent excellent results. There are, however, lesions such as the solid caseous focus which would not now be considered suitable for any form of collapse treatment.—*A propos de la résection segmentaire exérèse et collapsothérapie, M. Bérard, P. Juttin, & G. Maret, Poumon, August–September–October, 1953,* **9:** *493.—(F. S. Lansdown)*

**Segmental Resection.** Of 231 patients subjected to segmental resection between 1944 and July, 1953, 121 had tuberculosis; 14 had multiple resections. Among the tuberculous cases the commonest segments removed were the apico-dorsal, dorsal, and apical. Among the nontuberculous, the commonest were the basal pyramid, lingula, and right middle lobe. Segments were resected for mycoses (2 cases), benign tumors (3 cases), hydatid cysts (4 cases), chronic abscesses (15 cases), and bronchial dilatations and air cysts (51 cases). For the last, the entire bronchial tree must be mapped out preoperatively; an uninfected bronchiectatic area may reveal no visible or palpable abnormalities. Bronchograms should be repeated postoperatively to make sure that all diseased areas have been removed. From 83 operations, 8 of them bilateral, there were 78 cures, 2 deaths, and 2 incomplete results. There were 7 postoperative fistulas with empyema, all among the infected cases, and 5 incomplete expansions. Results were much less satisfactory in the infected cases even after prolonged preoperative treatment. In the 121 cases of tuberculosis, there were 103 successes and 18 failures, including 9 deaths. The commonest type of lesion resected was the solid caseous mass (43 cases), the second commonest being the ulcerocaseous lesion of limited extent (24 cases). Failure of the lung to reexpand was ascribed to (*1*) atelectasis of the operated lobe, which responded to bronchoscopic suction, (*2*) alveolar-bronchial escape of air, usually clearing spontaneously, or (*3*) bronchial fistula with empyema, which was most serious and caused 5 of the deaths. In every instance the bacilli had become streptomycin-resistant, the disease was insufficiently stabilized, or diseased bronchi had been transected. There were 8 local reactivations, 4 due to inadequate resection; and 6 contralateral spreads, one of them fatal. Functionally, as determined clinically and by testing, 7 patients were worse than before operation due to effusion or fixation of the diaphragm. Function was unchanged in 16 patients and improved in 5. Thus, segmental resection is benign and less mutilating than any other operation except thoracoplasty of 5 ribs or less. The indications must be precise and strict and it is difficult in tuberculosis to appreciate the exact extent of the involvement.—*Les résections segmentaires du poumon, O. Monod, Poumon, August–September–October, 1953,* **9:** *441.—(F. S. Lansdown)*

**Segmental Resection.**—If segmental resection carries no more risk than lobectomy and conserves more pulmonary function, it should be done whenever the topography of the lesion permits. The operative results following segmental resection for bronchiectasis have been identical to those following lobectomy. When the operation is performed for tuberculosis, however, the results have been otherwise. There was one fatality among 64 cases. Late results, after 56 operations, were good in 49 and incomplete in 4. There were 3 failures: one persistent empyema, one empyema requiring pleuropneumonectomy, and one em-

pyema and residual parenchymal lesion requiring pleuropneumonectomy. In some instances segmental resection may lead to complications which reduce pulmonary function to such an extent that the original purpose of the limited operation is defeated. Paradoxically, it is sometimes wise to perform a more radical operation for limited disease than for disease of greater extent; in the latter instance, one may have to be satisfied with removing only the most dangerous of many lesions.—*A propos des résections segmentaires pour tuberculose pulmonaire, J. Mathey, Poumon, August–september–October, 1953, 9: 485.*—(*F. S. Lansdown*)

**Indications for Segmental Resection.**—Segmental resection was performed for both tuberculous and nontuberculous lesions. Of the latter, single or multiple segments were removed for chronic abscess, bronchiectasis, cysts, and benign tumors. Of the tuberculous lesions, 3 types were resected: *First stage:* infiltrative processes which are dense, early, solitary, and usually caseous. These constitute a hazard and should be removed before they ulcerate. Undue haste should be avoided, however, and at least three to six months of absolute bed rest and chemotherapy should precede surgical intervention. *Second stage:* Cavities for which segmental resection is less justified and rarely realizable. The most common indications are cavities persisting after collapse therapy, traumatic pulmonary perforations, persistent bronchial perforations, and basal cavities. *Third stage:* Fibrotic scarring when lesions respond poorly to collapse therapy. They often prove amenable to segmental resection. Before undertaking resection, it is important to be assured that the bacilli are still sensitive to antimicrobials. Certain failures could be ascribed to bacterial resistance.—*Les indications des résections segmentaires, R. Monod & Germain, Poumon, August–September–October, 1953, 9: 431.*—(*F. S. Lansdown*)

**Behavior of Lobe After Segmental Resection.**—Following segmental resection, there are two groups of complications involving the remainder of the resected lobe: (*1*) immediate mechanical incidents and (*2*) late tuberculous complications. The mechanical accidents include escape of air from the permeable operated lobe, usually responding readily to continuous aspiration, and hematoma, either interlobular or parietopulmonary. When these are accessible, they should be evacuated. The tuberculous sequelae are more serious and indicate caution in selection of cases for segmental resection.—*Comportement postopératoire du restant lobaire après résection segmentaire pour tuberculose, Magnin & Perroil, Poumon, August–September–October, 1953, 9: 469.*—(*F. S. Lansdown*)

**Extrapleural Pneumothorax.**—During the past few years the prognosis of extrapleural pneumothorax has materially improved due to a number of factors: the availability of antimicrobial drugs for the control of infection, the return to simple extrapleural pneumothorax, the discontinuance of plombage, the use of streptokinase and streptodornase, and improvement in the technique of mobilizing the lung. Extrapleural collapse contributes to recovery by depriving the tubercle bacillus of oxygen, by providing rest and decreasing toxemia. Extrapleural collapse is a one-stage operation, non-deforming and well tolerated, even in poor risk patients with a low respiratory reserve. Contrary to past experiences, modern extrapleural collapse is largely a reversible procedure. Between 1947 and 1953, 134 operations were performed. There were 4 operative deaths; 11 operations were unsuccessful. Seven cases, reported in detail, demonstrate the usefulness of extrapleural collapse in acute progressive tuberculosis, uncontrolled hemoptysis, advanced bilateral disease, and in elderly and young patients.—*Modern extrapleural pneumothorax in the changing treatment of tuberculosis, J. W. Cutler, J.A.M.A., July 18, 1953, 152: 1096.*—(*H. Abeles*)

**Decortication.**—During the past four and one-half years, 51 decortication procedures have been done on 49 patients with pulmonary tuberculosis at the Nopeming Sana-

torium: in 30, for an unexpandable lung following pneumothorax; in 7, for tuberculous empyema; in 11, incidental to pulmonary resection to allow adequate expansion of the remaining portion of the lung; and in 3 patients, for miscellaneous conditions. Preoperative and postoperative courses of *p*-aminosalicylic acid and dihydrostreptomycin were used, as was preoperative bronchoscopy. No spread of disease appeared, but significant complications occurred in 10 patients. These were bronchopleural fistula and empyema in 2, thrombophlebitis in 2, persistent pneumothorax in 4, and hemothorax, wound abscess, and phrenic nerve injury in one each. In 28 cases the pleural space filled satisfactorily with decortication alone; 18 patients required thoracoplasty also. The average period between the onset of collapse and operation was a little more than twelve years. The initial extent of pulmonary disease influenced the necessity for thoracoplasty more than the duration of the collapse. Among 5 patients with fibrothorax and extensive mediastinal shift, only one had any postoperative return of the mediastinum to a normal position. Among 8 patients who had pre- and postoperative function studies, only one who underwent bilateral decortication showed improvement, 6 showed no improvement, and one became worse.—*Decortication in the treatment of pulmonary tuberculosis, F. H. Ellis, Jr., G. A. Hedberg, & V. R. Krueger, Proc. Staff Meet., Mayo Clin., September 23, 1953, 28: 537.*—(*E. A. Riley*)

**Modified Routine Chest Radiograph.**—The average roentgenographic image of the thorax does not completely fill a 14- by 17-inch radiograph. Approximately 4 inches of the film is noninforming in the subdiaphragmatic and superclavicular areas. By the use of sheet lead shielding and special attention to patient positioning, both the conventional sagittal radiograph and the apical lordotic view can be obtained on the same 14- by 17-inch radiograph.—*Technical modification of routine chest radiographs, R. W. Currie, J.A.M.A., July 25, 1953, 152: 1230.*—(*H. Abeles*)

## CLINICAL STUDIES, NONTUBERCULOUS DISEASES

**Bronchomotor Tone.**—Blood flow through the lungs might be intimately controlled by respiratory function through bronchiolar tone. Contraction of the bronchiole traps air in the alveoli, increasing air pressure, compressing the pulmonary capillaries, and inhibiting transudation across the capillary wall. Thus, increased bronchotonus can counteract pulmonary congestion and edema. When marked, increased bronchotonus may contribute to pulmonary hypertension and its sequelae. This thesis can be applied to several common clinical states. Many experimental techniques produce acute pulmonary edema, including intravenous injections of large doses of epinephrine or ammonium chloride, intracranial compression, and injection of veratrine or fibrin. These all may have a common mechanism. All increase the sympathetic activity and increase the amount of circulating adrenergic substances, or decrease parasympathetic tone. Epinephrine in appropriate doses overloads the left ventricle and simultaneously paralyses bronchomotor tone. Acute pulmonary congestion ensues as blood accumulates in the pulmonary veins and capillaries. If bronchomotor paralysis prevents a compensatory rise in the intra-alveolar pressure, transudation and pulmonary edema can be expected. Increased expiratory resistance may play a primary role in the pathogeneis of emphysema. When bronchiolar tone increases, air is trapped and the expiratory rise in intra-alveolar pressure is enhanced. This process may be cumulative until the lung is filled with air under tension. The alveolar capillaries are thereby compressed, some are obliterated and the blood flow through the lungs meets increased resistance. The trapped air reduces the effective pulmonary surface, with resultant cyanosis and hypoxia. Since acute hypoxia itself may raise intrapleural and pulmonary

arterial pressure, a vicious cycle is established. In severe hypoxia the effects of epinephrine are inhibited and those of acetylcholine are enhanced, furthering bronchospasm. The "rigidity" of the lung characteristic of this condition is dependent on entrapped alveolar air. The elastic tissues are not the primary offenders but are compressed and torn because of the primary bronchomotor disturbance. Right ventricular dilatation and hypertrophy occur if the increased bronchiolar tone and pulmonary hypertension are marked and persistent. Potent bronchodilaters, such as ephedrine, epinephrine and aminophylline may thus relieve cor pulmonale. The pulmonary arterial pressure falls despite increased cardiac output and pulmonary vascular resistance is markedly reduced. The pulmonary changes with pulmonary embolism are largely reflex. Embolic polypnea is not related to circulatory changes since it can be evoked by embolizing a bloodless lung. An embolus in an innervated lung, produces polypnea; occluding its pulmonary artery does not reduce the rate of breathing, but cutting the pulmonary branches of the vagus does. The intrapleural pressure increases markedly after embolism. Thus, reflex bronchiolar spasm is important in the embolized segment and radiates to the remainder of the lungs. Stretching of the precapillary arterial receptors by emboli sets off generalized reflexes which normally prevent pulmonary engorgement. Increased bronchiolar tone results; excessive, alveolar gas exchange is impeded, cyanosis develops, and acute right heart failure may result from the suddenly increased load on the right ventricle. The bronchomotor concept also explains certain aspects of congestive heart failure. When the left ventricle cannot pump away the pulmonary venous return, there is progressive pulmonary congestion, transudation, and edema; frank pulmonary edema does not necessarily ensue at once. Reflex bronchoconstriction may increase the pulmonary resistance and so transfer the burden to the right ventricle. Disturbed respiration, such as paroxysmal nocturnal dyspnea, may be a manifestation of these compensatory mechanisms; in congestive failure, the intrapleural pressure is elevated as is the pulmonary arterial pressure. As the transudate is forced from the alveoli, the lungs become dry and piping expiratory rales are heard. If bronchiolar tone becomes excessive, as may occur in hypersensitive persons or those with chronic bronchitis, the asthmatic tendency may predominate as cardiac asthma. Paroxysmal nocturnal dyspnea may, therefore, be considered as the antipode of cardiac asthma rather than its synonym, even when both appear during the same attack.—*Bronchomotor tone, S. Rodbard, Am. J. Med., September, 1953, 15: 356.*—(*T. H. Nochren*)

**Lung Musculature in Disease.**—It has become increasingly obvious that the lungs are muscular organs. Pathologic muscular hypertrophy and hyperplasia in the lung were recognized in 1872, but little is known of the origin, distribution, and functional import of the muscular tissue in pulmonary disease. Hence, a study was made of sections of lungs containing an unusual amount of muscle. The tissues were obtained from routine necropsy material and surgical specimens. From 426 specimens, 40 were selected for special study. More than half of the latter came from cases of emphysema and bronchiectasis; cases of abscess and bronchitis (asthma) were also frequent. The hypertrophy and hyperplasia of muscle was often remarkable. Much of this muscle was derived from (*1*) bronchi and more distal air spaces, (*2*) blood vessels, especially the longitudinal layer of the bronchial arteries, (*3*) lymphatics, or (*4*) interstitial tissue not clearly associated with other structures. Muscle fibers from these sources became commingled. In vessels, the lumen sometimes was completely obliterated by muscular hyperplasia, thus abolishing a useless or even burdensome collateral circulation. Hyperplasia was especially striking in some cases of pulmonary emphysema; the walls of the bullae contained masses of myoid tissue from all of the sources. Residual cells became compact as tissue was destroyed and bullae developed, in part accounting for the abundant muscle in the walls. Bronchioles leading to the em-

physematous region sometimes had great collars of muscle and narrow lumina, perhaps obstructing them and producing emphysema. This muscle may be relaxed by certain drugs and relieve the symptoms of some patients with this condition, but its response should be further studied. Mechanisms responsible for the muscular hypertrophy and hyperplasia are not fully understood; entrapment of fibers at increased tensions, especially in tissue undergoing fibrosis may play a role.—*The musculature of the lungs in chronic pulmonary disease, A. A. Liebow, W. E. Loring, & W. L. Felton, II, Am. J. Path., September–October, 1953, 29: 885.—(J. S. Woolley)*

**Bronchostenosis and Asthma.**—Of 1,034 consecutive asthmatic patients who underwent bronchoscopic examination, 327 had stenosis of one or more bronchi. There were 182 female and 145 male patients in this group, the youngest one being three years of age and the oldest seventy-four. The most prominent findings were cough and fever; 35 per cent of the patients had hemoptysis. An upper respiratory infection preceded the attack of bronchostenosis in 50 per cent of the cases; pleurisy on the affected side had occurred in 32 per cent. In only 30 per cent of the cases were the thoracic roentgenograms of value in diagnosing bronchostenosis. There were no clinical means except bronchoscopic observation to determine whether benign bronchostenosis existed. Dilatation and aspiration alone usually gave prompt relief. The incidence of bronchostenosis was far higher in the right than in the left lung. The superior division of the lower lobe was most frequently involved. Two patients died after bronchoscopy. In 13 of the 327 patients with bronchostenosis, subcutaneous emphysema developed after bronchoscopy with dilatation. Immediate improvement after dilatation of the stenosed bronchus occurred in 60.5 per cent of the patients, delayed improvement in 63.6 per cent, and sustained improvement in 60.5 per cent. The corresponding figures in a control group of asthmatic patients without evidence of stenosis on bronchoscopy were 55 per cent, 48 per cent, and 45 per cent, respectively.—*Bronchostenosis complicating asthma, T. W. Mears, L. E. Prickman, & H. J. Moersch, J.A.M.A., July 11, 1953, 152: 997.—(H. Abeles)*

**Necrotizing Granulomatosis of Lungs.**—Six cases of chronic pneumonitis of the cholesterol type and one case of idiopneumonic necrotizing granulomatosis and angiitis were compared with 2 other cases of the latter type previously reported. In all of these cases, the lesions were often subpleural masses. There were ulceration and obstruction of the bronchioles and small bronchi, fibroblastic proliferation, collagen deposition, and vacuolated macrophages filled with cholesterol-rich lipid. Idiopneumonic necrotizing granulomatosis appeared to be a transition between chronic pneumonitis of the cholesterol type and disseminated necrotizing granulomatosis and angiitis. The primary disorder in pneumonitis of the cholesterol type may be ulceration and obstruction of the smaller branches of the bronchial tree; intra-alveolar macrophages filled with cholesterol-rich lipid thus may appear secondarily. These changes in the smaller branches of the bronchial tree may be caused by a hypersensitivity phenomenon less intense than that responsible for idiopneumonic and disseminated necrotizing granulomatosis and angiitis. This may represent an Arthus reaction localized in the bronchial tree. The cause of the sensitization is unknown.—*Necrotizing granulomatosis and angiitis of the lungs and its relationship to chronic pneumonitis of the cholesterol type, R. Fienberg, Am. J. Path., September–October, 1953, 29: 913.—(J. S. Woolley)*

**Sarcoidosis of Skeletal Muscle.**—Sarcoidosis, or Boeck's sarcoid, has been described in nearly every tissue, but sarcoid lesions in skeletal muscle have been described in only 18 reported cases. Another 3 cases of sarcoidosis involving skeletal muscle were recently seen at Duke University, where there have been 4 earlier cases, one of which was previously reported. Thus, 24 cases are now reported. The muscular lesions were detected clinically in

approximately half of the cases, most commonly as nodules, particularly in the muscles of the extremities (7 cases). In 3 of the present cases, "subcutaneous nodules" were described clinically; microscopically, skeletal muscle was also involved. The nodules were sometimes associated with weakness, soreness, or atrophy, but often there were only the nodules. The clinical picture may simulate muscular dystrophy. Of the 7 autopsied cases, 6 also had myocardial sarcoidosis, suggesting a direct relationship between myocardial and muscular sarcoidosis. In one patient with complete heart block, post-mortem study showed sarcoidosis of the myocardium and of the walls of the great veins.—*Sarcoidosis of skeletal muscle: Report of 6 cases and review of literature, L. W. Powell, Jr., Am. J. Clin. Path., September, 1953, 23: 881.—(J. S. Woolley)*

**Tuberculosis and Leprosy.**—A study was carried out in Eastern Nigeria to determine the incidence of positive tuberculin and lepromin skin tests. Among 81 children tested between the ages of one and fifteen, 47 (58 per cent) were tuberculin-positive and 31 (35 per cent) lepromin-positive. Among 278 adults tested, 223 (80.2 per cent) were tuberculin-positive and 224 (80.5 per cent) were lepromin-positive. The high percentage of natives who reacted positively to both tests (22 per cent of the children and 64.6 per cent of the adults) could mean that exposure to a tuberculous infection usually causes the lepromin test to become positive. This hypothesis was tested by giving BCG to 65 tuberculin-negative natives, all except 7 of whom were lepromin-negative; 64 became tuberculin-positive. Among the 58 natives previously lepromin-negative, 40 became positive and 14 became doubtful. Only 3 subjects who became tuberculin-positive did not become lepromin-positive. Since a positive lepromin reaction is generally accepted as indicating some immunity to leprosy, the use of BCG is endorsed in areas where leprosy is common and difficult to control.—*Tuberculosis and leprosy: Immunological studies in healthy persons, J. Lowe & F. McNulty, Brit. M. J., September 12, 1953, No. 4836: 579.—(E. A. Riley)*

**Syncope and Coughing.**—Syncope from coughing is common and results from an acute diminution of blood pressure to the brain. Continuous records in 27 cases indicated that only normal physiologic mechanisms were involved. The violence of the coughing was the determining factor, intrathoracic pressures of 200 to 300 mm. of mercury being reached. Subjects who coughed continuously without drawing breath had circulatory changes which were exaggerated examples of the effects of the Valsalva maneuver. Consciousness was usually lost during the period of acute hypotension just after coughing. Occasionally, syncope occurred while intrathoracic pressure was still high, but the arteriovenous pressure difference across the brain was greatly reduced. Subjects who coughed intermittently also had syncope. Arterial pressure and peripheral blood flow records showed vasodilatation following this form of coughing in contrast to the vasoconstriction which resulted from the Valsalva maneuver and continuous coughing. It is suggested that vasodilatation following intermittent coughing is due to the stimulation of baroceptors by large arterial cough transients. Intrathoracic pressure remained elevated about 10 mm. of mercury for many seconds following intermittent coughing (Author's summary).—*The mechanism of syncope after coughing, E. P. Sharpey-Schafer, Brit. M. J., October 17, 1953, No. 4841: 860.—(E. A. Riley)*

**Smoker's Syndrome.**—Smoker's "asthma" is characterized by a triad of symptoms: chronic pharyngitis, wheezing and dyspnea, and a tendency to respiratory infections, with and without fever. This was observed in 58 patients; 28 recovered completely when they stopped smoking, 24 when they quit smoking and were given antibiotic treatment. The most characteristic and constant feature is chronic inflammation of the pharyngeal mucosa and tonsillar area. The pharyngeal mucosa shows persistent hyperemia with small lymphoid nodules on the pharyngeal wall. Asthma-like

wheezing, cough, and expectoration are most pronounced in the morning, not, as might be expected, when the patient smokes most. Dyspnea occurs on exertion in approximately half of the patients. It is usually not intense, but in some cases dominates the clinical picture. Chest pains are rhythmic, darting, and angina-like; they occur in any part of the lungs or around the heart and hypogastrium, radiating into the neck and arms. They are associated with a sensation of precordial constriction. The history of frequent respiratory infections is borne out by roentgenograms, which reveal increased hilar markings, scar formation, and pleural adhesions. In some instances infiltrates suggest cancer but disappear upon treatment. This condition may lead to chronic emphysema and so-called "intrinsic asthma" following persistent infections of the upper respiratory tract. When allergic asthma is complicated by this syndrome, the asthma does not yield to allergic management unless the patient abstains from smoking.—*Smoker's respiratory syndrome, G. L. Waldbott, Ann. Int. Med., November, 1953, 39: 1026.*—(*T. H. Noehren*)

**Chest Findings in Hemorrhagic Fever.**—The roentgenographic findings in hemorrhagic fever consist of pulmonary congestion, both central and focal. The central type of pulmonary congestion is demonstrated by wide pulmonary vascular markings at the hili with increased linear densities fanning outward into the lungs. Associated with this there may be numerous patchy areas of congestion in the lungs which may be confluent. Cases also are seen in which focal areas of congestion in the periphery of the lung are present without evidence of hilar vascular congestion. The central type of congestion is thought to be due primarily to renal failure of the lower nephron type, evidenced by oliguria with azotemia followed by polyuria and hyposthenuria. In these patients clearing of the chest, as seen on the roentgenogram, correlates well with improvement of kidney function.—*Roentgenologic observations in hemorrhagic fever, D. W. S. Stiff & G. M. Powell, Radiology, November, 1953, 61: 807.*—(*W. J. Steininger*)

**Effect of Virus on Exfoliated Cells.**—Several viruses can inhibit the growth of transplantable tumors in animals. Bunyamwera and West Nile viruses have inhibited the growth of certain mouse ascites tumors, and exfoliated cells in the ascitic fluid demonstrated the oncolytic effect. This suggested a study of ascitic and pleural effusions from patients undergoing experimental clinical virus treatment. Six patients with inoperable cancer were treated with Egypt 101 and Egypt 21 strains of West Nile virus. The exfoliated cells in the pleural and peritoneal fluids were evaluated as to the percentage of malignant and non-neoplastic cells according to the Papanicolaou technique. Fewer neoplastic cells were exfoliated in 2 patients following inoculation of the virus; one had terminal bronchiolar carcinoma, the other had lymphosarcoma. Following viral infection, lymphocytes increased in the effusions of 6 of the 5 patients with carcinoma. Although certain factors limit its use, the Papanicolaou technique for studying serial specimens of serous effusions offers a method for evaluation therapeutic efficacy.—*Morphological changes of exfoliated cells in effusions of cancer patients following induced viral infections; Preliminary observations, I. Koprowska, Am. J. Path., November–December, 1953, 29: 1105.*—(*J. S. Woolley*)

**Acute Respiratory Disease in Children.**—Acute respiratory infection in children should be classified according to the anatomic distribution of the infection; in most instances, the infection is so complex, involving both bacteria and viruses, that an etiologic classification is impractical. The anatomic situation most affects the patient's respiratory function and the clinician can usually locate the infection by history and physical examination. Two controversial conditions, "primary atypical pneumonia" and "primary virus pneumonitis of infancy," probably are caused by the synergistic effect of bacteria normally in the upper respiratory tract and various poorly

known viruses. Infinitely variable bacterial and viral admixtures may produce markedly variable syndromes and they may be better called "mixed pneumonias."—*Acute respiratory disease, with special reference to pathogenesis, classification, and diagnosis, G. Manson, J. Pediat., November, 1953, **43:** 599.—(M. J. Small)*

**Pulmonary Tularemia.**—A tumor-like opacity was observed in the apical segment of the left lower lobe of a patient who had presumably been exposed to tularemic infection twelve to eighteen months previously. The clinical course was protracted over two and a half to three years, and was followed by recovery. The retrospective diagnosis was based on the history, which indicated that the patient had stayed in a region where tularemia is endemic, and on an agglutination test and positive skin reaction for tularemia.—*Über eine Spätform der pulmonalen Tularämie, K. Inhäuser, Deutsche med. Wchnschr., July 17, 1953, **29–30:** 1020.—(L. Molnar)*

**Trypsin Inhalations.**—Crystalline trypsin is fibrinolytic and can digest respiratory mucin, suggesting its value for treating bronchial disorders associated with hypersecretion and accumulation of fibrinomucinous sputum. Seventy-three patients with respiratory conditions, with or without thick, viscous sputum were treated with trypsin in aerosol form. The initial dose was 75,000 units, followed by 100,000 and 125,000 units for various periods. Each 50,000 units were dissolved in 1 ml. of Sorensen's phosphate buffer solution. Before the inhalation, the patient was usually given 0.25 ml. of a 1:1,000 solution of epinephrine combined with 0.75 ml. of a soluble antihistaminic agent. The "mask" method of aerosolization was used although aerosols may be given by the direct method using oxygen, the direct method using compressed air, or the direct method using a hand pump. The results of aerosol trypsin were excellent in 14 of 19 cases of bronchiectasis, with or without bronchial asthma; in 4 of 5 cases of acute atelectasis; in 7 of 11 cases of bronchial asthma with infectious bronchitis or pneumonitis; in 4 of 7 cases of paroxysmal bronchial asthma; and in 5 of 31 cases of chronic bronchial asthma with emphysema. It was also used successfully in 5 of 8 cases of bulbar poliomyelitis with tracheotomy. There were 20 untoward reactions among the 73 patients who received 270 trypsin aerosol inhalations. They consisted of transient hoarseness, increased asthma, rash about lips, and nausea and vomiting.—*Trypsin inhalations in respiratory conditions with thick sputum, L. Unger & A. H. Unger, J.A.M.A., July 18, 1953, **152:** 1109.—(H. Abeles)*

**Automatic Aerosol Device.**—A modification of the Miller apparatus for continuous aerosol therapy has the advantage of requiring less attention and providing a method for administering an aerosol to a patient for twenty-four hours or longer with minimal attention.—*Completely automatic Miller aerosol device, C. M. Trossman, Am. J. Dis. Child, October, 1953, **86:** 436.—(M. J. Small)*

**Treatment for Neonatal Atelectasis.**—Atelectasis in the newborn infant is occasionally due to underdeveloped ribs and costal cartilages. The high negative intrathoracic pressures required to overcome the cohesion of the moist alveoli surfaces of the atelectatic lung cannot be attained without assistance in these infants. A traction method of sternal stabilization, similar to that used in adults with fractured ribs and sternum, is advised for treating newborn infants who manifest sternal retraction and cyanosis in the neonatal period. The skin and fascia overlying the lower end of the sternum are caught with a towel clip. Traction is applied through small rubber bands attaching the handle of the towel clip to the top of the incubator. An additional clip or clips can be placed on the skin and fascia overlying the ribs if this seems necessary to control retraction. The response is frequentiy immediate with gratifying disappearance of cyanosis and a striking increase in the effectiveness of inspiration.—*New treatment for atelectasis of the newborn, W. G. Love,*

*Jr., & B. Tillery, Am. J. Dis. Child., October, 1953, 86: 423.—(M. J. Small)*

**Idiopathic Pericarditis.**—In a study of the clinical and laboratory features of 28 cases of acute benign pericarditis, no case was considered idiopathic until all known causes, such as rheumatic fever, tuberculosis, myocardial infarction, uremia, tumor, trauma, or specific infections, could be eliminated. The results of tuberculin skin tests paralleled the usual incidence in the patient population. Two patients had a unilateral, right-sided effusion, but each had a negative Mantoux test using second-strength purified protein derivative. Pericardial fluid, obtained by aspiration from 4 cases, was an exudate with a specific gravity of 1.019 to 1.023; it contained many cells, 80 to 95 per cent of which were lymphocytes; the total protein content varied from 4.5 to 6.0 gm. per 100 ml. Cultures and smears were negative, but the pericardial fluid could be bloody. Pericardial biopsy was obtained in one case and showed nonspecific inflammatory changes. In making a differential diagnosis, tuberculosis can be identified by the more severe systemic reaction, the prolonged course, the signs of tuberculosis elsewhere, and the positive Mantoux skin test, most of which were not present in the cases of acute idiopathic pericarditis. Other causes of acute chest pain, such as dissecting aneurysm, angina, hiatus hernia, spontaneous pneumothorax, mediastinal emphysema, acute pleurisy, pulmonary infarction, seldom cause difficulty in the differential diagnosis after complete physical and laboratory examination.—*Acute idiopathic pericarditis, E. M. Goyette, Ann. Int. Med., November, 1953, 39: 1032.—(T. H. Noehren)*

**Electrolyte Studies in Pericardial Resection.**—Studies were conducted in 2 cases of pericardial resection for constrictive pericarditis. During the eight days of balance studies before operation, there was a cumulative deficit of 55 gm. of salt, chiefly through aspiration of pleural fluid. Hyponatremia occurred and the total urinary sodium excretion for the seventy-two hours prior to operation was only 25 milliequivalents despite the repeated use of a mercurial diuretic. Hypotension developed while blood was being received and continued in spite of replacement of the estimated blood loss. Values for the hematocrit and blood and plasma volumes obtained during the period of hypotension did not indicate the presence of inadequately treated hemorrhage. Hypotension and oliguria were overcome at approximately the time the sodium deficit was corrected. It is concluded that, in preparing cardiac patients for surgery, the possibility of deleterious effects from sodium depletion following a limited salt intake and the abnormal loss of body fluids must be considered. In discussing this paper, H. Black stated that formerly his postoperative cardiac patients were given hypertonic sodium chloride when a low serum sodium value was associated with clinical features of the "low sodium syndrome," that is, hypotension, apathy, and disorientation. On many occasions this therapy was coincident with a rapid correction of the clinical aberrations and a rise in the serum sodium concentration. In a few cases the salt aggravated congestive failure, with a fatal result in at least one instance. The routine was therefore modified by restricting patients to 1,500 cc. of fluid, other than blood, on the first, second, and third days. The ration was not increased until usual spontaneous diuresis occurred except in hot weather. With this method few patients experienced the severe drop in sodium concentration formerly seen and it was not necessary to use hypertonic salt solution. On the basis of these total balance studies, he believed that the administration of saline solution to cardiac patients preoperatively or postoperatively usually is not rational and may be dangerous. —*Electrolyte studies in pericardial resection, W. B. Crandell, A. Yeomans, D. L. Hoffman, & G. H. Stueck, Jr., J. Thoracic Surg., November, 1953, 26: 486.—(R. E. MacQuigg)*

**Pulmonary Arteriovenous Fistula in Siblings.**—Serious complications may develop in patients with pulmonary arteriovenous fistula

and more than one sibling in a family may have the condition. In 2 sisters the diagnosis was established from angiocardiograms. Both patients were essentially asymptomatic, the lesion being discovered on routine chest roentgenogram. Profound clinical changes occur in peripheral arteriovenous fistulas, and it is important that such changes are often absent in pulmonary arteriovenous fistulas. Roentgenographic demonstration of a pulmonary lesion with further study by angiocardiography is the surest method of diagnosis. While the pulmonary arteriovenous aneurysm is actually an arteriovenous fistula, there are frequently no signs or symptoms perhaps because the vascular resistance of the lung is low. The treatment of choice is excision even if the patient is asymptomatic. Several cases have shown that these lesions tend to progress, often with alarming rapidity. Besides the expected cardiovascular and respiratory embarrassment, other more subtle complications, such as brain abscess and fatal hemoptysis, may be equally disastrous. The risk of surgical removal of a pulmonary arteriovenous fistula seems much less than that of complications if the fistula is left alone.—*Pulmonary arteriovenous fistula occurring in siblings, F. Glenn, C. S. Harrison, & I. Steinberg, Ann. Surg., December, 1953, **138:** 886.—(M. J. Small)*

**Anomalous Pulmonary Veins.**—In a postero-anterior chest roentgenogram, a crescentic, saber-shaped vascular shadow sometimes runs downward, parallel to or behind the right side of the heart and disappears in the region of the right cardiophrenic angle. It probably represents a vein drawing blood from the right lung into the right atrium or inferior vena cava. Other suggestive findings are a variable shift of the heart into the right hemithorax, a small right hemithorax, possibly due to diminished function of the anomalously drained right lung, a rather characteristic shape of the right cardiac border, a small or even invisible aorta, and a large pulsating pulmonary artery. In some instances the pulmonary artery may be small or even absent. Cardiac catheterization studies will often prove conclusively that anomalous pulmonary drainage exists.—*Roentgenologic findings in anomalous pulmonary venous connections, A. Brower, Proc. Staff Meet., Mayo Clin., August 26, 1953, **28:** 480.—(E. A. Riley)*

**Anomalous Pulmonary Venous Connection.**—A case of partial anomalous pulmonary venous drainage was treated surgically by an anastomosis between the anomalous trunk and the left atrium. The postoperative course was uneventful and the patient showed considerable symptomatic improvement. This is the first surgically corrected case reported in the literature.—*Surgical treatment of anomalous pulmonary venous connection, J. W. Kirklin, Proc. Staff Meet., Mayo Clin., August 26, 1953, **28:** 476.—(E. A. Riley)*

**Partial Anomalous Pulmonary Venous Return.**—A partial anomalous pulmonary venous connection may present widely divergent clinical pictures usually judged to represent an atrial septal defect. Anomalous drainage into the right atrium or tributaries results in a pulmonary recirculation of oxygenated blood proportional to the number of lobes drained. The condition is serious largely because of increasing strain on the right side of the heart which must maintain a flow equal to the systemic output plus the volume of recirculated blood. Complications depend largely upon whether an atrial septal defect is present and upon its size. With an intact septum, removal of the normally drained lung would be fatal: with a septal defect, survival would be theoretically possible. Partial anomalous pulmonary venous drainage is relatively benign and, if severe disability in childhood results, an associated septal defect may be present. The routine history and examination are generally diagnostically inconclusive. In 2 cases the findings at cardiac catheterization and arterial dye-dilution studies led to the diagnosis.—*Clinical considerations in partial anomalous pulmonary venous connection: Report of two unusual cases, H. T. Mankin & H. B. Burchell, Proc. Staff*

*Meet., Mayo Clin., August 26, 1953, 28: 463.—(E. A. Riley)*

**Absence of Pulmonary Artery.**—Two cases of isolated congenital absence of a main branch of the pulmonary artery were asymptomatic, and there was only mild respiratory and cardiovascular disability observed on pulmonary function and cardiac catheterization studies. The ages of the patients, fifty-three and twenty-six years, and their continued well-being during follow-up examination suggest that the prognosis is favorable, barring any complicating disease of the "good" lung. The diagnosis may be suspected when conventional roentgenograms of the chest reveal overdistention and mediastinal herniation of one lung with hypoplasia and diminished vascularity of the affected lung. Absence of a main pulmonary artery branch is demonstrated by angiocardiography.—*Congenital absence of a main branch of the pulmonary artery, I. Steinberg, C. T. Dotter & D. S. Lukas, J.A.M.A., July 25, 1953, 152: 1216.—(H. Abeles)*

**Abruption of the Lung.**—Agenesis of the lung is very rare; hypoplasia of the lung occurs more often, but abruption of the bronchial stem of the lung is still rarer than agenesis. In the case of an airless lung, it is difficult to find the cause. Diagnosis post mortem is easier than diagnosis during life, but with present roentgenographic techniques, bronchoscopy, bronchography, and arteriopneumography, ante-mortem diagnosis is possible. A 31-year-old man, born a normal child, fell from his father's arms when five months old, struck the edge of the crib, and bled profusely from his nose. From that time on, he had recurrent bleeding and, later, green pus from the nose. His development was considerably retarded and he was unable to finish public school because his breath was so repulsive. Skiagraphic examination revealed a homogenous shadow covering the entire left side of the chest. Bronchography showed a stump about 1 cm. wide and 5 cm. long in place of the left bronchus. Multiple scars and the end of the bronchus were clearly visible at the bronchoscopic examination. Angiography demonstrated a well-developed pulmonary artery on the right and only the shadow on the left.—*A contribution to the differential diagnosis of agenesis and abruption of a lung (Czech), J. Munz, Lék. listy, August 1, 1953, 8: 348.—(J. Ilavsky)*

**Superior Vena Caval Obstruction.**—Superior vena caval obstruction in a patient with bronchogenic carcinoma is an ominous event, heralding inoperability, producing severe discomfort, and curtailing useful activity. Such obstruction occurred in 15 per cent of a series of patients with bronchogenic carcinoma, was most frequent with lesions of right bronchial origin (80 per cent), and nearly always was associated with anaplastic bronchial neoplasms (90 per cent). The blood flow is interrupted by the primary bronchial neoplasm or invaded lymph nodes, principally through external compression, occasionally by intraluminal invasion, and rarely by thrombosis. The degree of disability and immediate prognosis depend upon the efficiency of the collateral circulation. The site and nature of the obstruction as well as the pattern of collaterals can best be determined by phlebography or angiocardiography. Unless decompression therapy is promptly and effectively instituted, superior vena caval obstruction progresses rapidly. In a series of 58 such cases, roentgen therapy and/or nitrogen mustard gave striking palliation and prolonged useful activity. Roentgen therapy is the treatment of choice, with nitrogen mustard as an adjunct when irradiation is unfeasible or ineffective.—*The superior vena cava obstruction syndrome in bronchogenic carcinoma: Pathologic physiology and therapeutic management, B. Roswit, G. Kaplan, & H. G. Jacobson, Radiology, November, 1953, 61: 722.—(W. J. Steininger)*

**Endocardial Fibro-Elastosis.**—Endocardial fibro-elastosis, also called endocardial sclerosis and fetal endocarditis, is particularly important in connection with corrective cardio-

vascular surgery; it may produce cyanosis but cannot be surgically corrected by present methods. In endocardial fibro-elastosis, there is cardiac enlargement due both to hypertrophy of the myocardium of the left ventricle and dilatation as a result of failure. The endocardium of the left ventricle is thickened and fibrotic. Valvular changes consisting of contractures, thickening of the valve leaflets, and occasional adhesions of the leaflets can sometimes be seen. Microscopically the endocardium reveals fibrous and elastic tissue thickening without evidence of inflammation. The disease occurs primarily in infancy and childhood; most patients die before the age of six months. The major symptoms include dyspnea, listlessness, vomiting, and occasionally cyanosis. There may be peripheral edema. In an infant or young child with (*1*) an episode of left heart failure, usually following an upper respiratory infection, (*2*) electrocardiographic evidence of marked left ventricular hypertrophy and anoxemia, and (*3*) roentgenographic findings of gross cardiac enlargement, predominantly left ventricular, a presumptive diagnosis of endocardial fibroelastosis may be made.—*Endocardial fibroelastosis, M. N. Golper, Radiology, December, 1953, 61: 865.—(W. J. Steininger)*

**Mitral Valvotomy.**—The basic indication for mitral valvotomy is disability from mitral stenosis of an anatomic form which is amenable to surgical correction. This type of stenosis, in which there is a pliant diaphragmatic valve, gives rise to characteristic clinical signs by which it may be recognized. The most important consequence of pulmonary hypertension is right ventricular enlargement; and the size of the right ventricle, as determined by clinical, radiographic, and electrocardiographic findings, provides a more valuable index to the degree of pathologic change due to mitral stenosis than does the level of the pulmonary arterial pressure at a given moment. Cardiac catheterization is no longer required as a routine measure in the selection of cases suitable for mitral valvotomy. Selection may now be made on a basis of the symptoms and of the data provided by routine cardiologic examination. Mitral valvotomy has been performed on 150 patients, of whom 31 were men and 119 women. Their ages ranged from nineteen to fifty-seven years. Four patients died as a direct result of the operation, an immediate mortality of 2.7 per cent. Four patients died from various causes some time after the operation. The results in 111 patients followed for five months to two and a half years have been good in 74 per cent and only fair or poor in 20 per cent. Patients with auricular fibrillation (41 per cent of the series) did as well as those in sinus rhythm, but 3 of the 4 operative fatalities were in fibrillating patients. Cases selected for operation on grounds of an operable valve were classified according to the size of the right ventricle and the presence of congestive failure. Patients with large hearts and congestive failure which failed to respond to treatment benefited least from valvotomy. When free splitting of the commissures was achieved, 84 per cent of the patients obtained good symptomatic relief, whereas, when valvotomy was judged at the operation to be less satisfactory, only 46 per cent of good results were obtained. Nevertheless, partial splitting of the valve does not preclude satisfactory clinical improvement. Good results were obtained alike in those with greatly elevated pulmonary arterial pressures and in those with a slight or moderate elevation. The following are regarded as contraindications to operation: active rheumatic carditis, severe myocardial damage as revealed by gross right ventricular enlargement and intractable congestive failure, predominant aortic valve disease, organic tricuspid valve disease, mitral incompetence associated with left ventricular enlargement and a giant left auricle. Chronic bronchitis, emphysema, and other pulmonary complications prejudice the success of the operation. (Authors' summary).—*Valvotomy in the treatment of mitral stenosis, T. H. Sellors, D. E. Bedford, & W. Somerville, Brit. M. J., November 14, 1953, No. 4845: 1059.—(E. A. Riley)*

**Commissurotomy and Pulmonary Function.**—Pulmonary function has been studied in 9 cases of mitral stenosis before and after commissurotomy. The patients were from the wards of the Walter Reed Army Hospital and had evidence of uncomplicated mitral stenosis which had led to progressive dyspnea and/or hemoptysis. In each instance the diagnosis was confirmed at the time of commissurotomy. Before operation, several cases showed an increase in the effective shunting of venous blood through unaerated or poorly ventilated lung with, in some instances, arterial unsaturation. This abnormality was largely corrected by commissurotomy. Pulmonary diffusing capacity was frequently impaired, little affected by operation, but usually not sufficiently reduced to cause lowering of arterial oxygen tension during the breathing of room air. Resting hyperventilation, when due to pulmonary congestion, was diminished after commissurotomy.—*Pulmonary function studies in mitral stenosis before and after commissurotomy, M. H. Williams, Jr., J. Clin. Investigation, November, 1953, 32: 1094.*—(*E. Dunner*)

**Bronchial Cyst with Anomalous Artery.**—Bronchial cysts (sequestrated lung, congenital bronchiectasis, lower accessory lung) accompanied by an anomalous artery are sufficiently frequent to be of clinical interest. This artery may bleed if it is overlooked, and its possible existence must be remembered at each operation. The sequestrated pulmonary tissue is almost invariably in the lower lobe or outside the lung in the lower part of the pleural cavity; it is functionally detached from the normal lung by developmental defect or by disease, usually as a bronchial cyst or bronchiectasis. Sequestra may be within the lung (intralobar), outside the lung and covered with pleura, in the mediastinum or abdomen (abdominal lung). They are discovered by roentgenographic examination when the chest is investigated following pneumonia or other respiratory infection. The diagnosis of empyema or abscess is sometimes made, and treatment of these conditions is instituted, the true nature of the disease not becoming apparent until later. Resection of the cyst, lobectomy, or even pneumonectomy is indicated to prevent chronic recurring pulmonary disability. In one case, a cyst of the right lower lobe had a pedicle leading to the abdomen. During its dissection, alarming hemorrhage occurred. The cyst was lined with ciliated bronchial epithelium, and the hollow structure of the pedicle was an artery 4 mm. in diameter. The cystic mass did not communicate with the hilar bronchi. The air-fluid level of this cyst in the roentgenogram probably resulted from metabolic gas. This is the twelfth reported instance of an abnormal artery arising below the diaphragm to supply pulmonary tissue in the thorax. Lung sequestra probably arise from a source distinct from that of the origin of the normal lung.—*Bronchial cyst associated with anomalous artery, W. F. Fry, H. S. Arnold, & E. W. Miller, Ann. Surg., December, 1953, 138: 892.*—(*M. J. Small*)

**Bronchiectasis.**—Of 36 cases of bronchiectasis in children, a pure or almost pure infection by *H. influenzae* was present in 35. Chloramphenicol, to which this organism is highly sensitive, invariably produced a remission while being given in adequate doses. After cessation of treatment, severe cases reverted to their original condition but some milder ones appeared to have received more lasting benefit. One patient died of aplastic anemia, an occurrence which led to the abandonment of the treatment (*Authors' summary*).—*Chloramphenicol treatment of bronchiectasis in children, A. W. Franklin & L. P. Garrod, Brit. M. J., November 14, 1953, No. 4845: 1067.*—(*E. A. Riley*)

**Resection for Bronchiectasis.**—From March, 1948, to July, 1952, 52 patients with bronchiectasis and congenital cystic lungs were operated upon at Palacky's University in Olomouc. There were 25 women and 27 men; 40 of them were less than thirty years of age. The main complaint of these patients was expectoration of huge volumes of putrid,

bad-smelling sputum. They also had progressive toxic cachexia, secondary anemia, tiredness, inability to perform physical work, seek amusement, and so on. Almost all of the patients had been treated by various conservative methods; most responded favorably to chemotherapy, but only briefly. Bronchiectasis was diagnosed by clinical symptoms as well as by the results of roentgenographic, endoscopic, and laboratory examinations. To ensure smooth postoperative healing, the patients were carefully prepared for operation by diminishing pyogenic and putrid secretions to a minimum and enhancing the patient's strength. Blood transfusions, cardiotonics, aerosol inhalations, respiratory exercises, enforced coughing to increase expectoration, and bronchial drainage were most frequently used for that purpose. Among the 52 patients, 49 had bronchiectasis and 3 had congenital cystic lungs. Of the 53 resections, 4 were segmental, 21 were lobectomies, 9 lobectomies with lingulectomies, 11 bilobectomies, and 8 pneumonectomies. Two patients (3.8 per cent) died after the operation. Segmental resection was always performed from the hilus toward the periphery. The surgeon intermittently applied moderate traction to the bronchiovascular stem and pressed gauze or finger upon the parenchyma. The affected segment was thus removed relatively quickly and carefully. Lower lobectomies were performed as usual, the bronchus being cut close to the main stem to leave as short a stump as possible. The incidence of postoperative complications was surprisingly low.—*Resection of the lung in bronchiectasis (Czech), Z. Šerý & P. Lisoněk, Lék. listy, April 15, 1953, 8: 176.*—(*J. Ilavsky*)

**Hemopneumothorax.**—Patients with simple spontaneous pneumothorax usually recover, but the mortality rate of hemopneumothorax approaches 25 per cent. Death usually occurs during the first twenty-four to forty-eight hours, and the prognosis is excellent if the patient survives the acute episode. Blood in the pleural space, however, can cause an inexpansible lung as fibrin deposits and organizes on it. Decortication then is usually necessary. Thus, spontaneous hemopneumothorax is potentially a grave emergency requiring early and energetic therapy. Treatment should include: (*1*) early and complete removal of both blood and air; (*2*) early thoracotomy, with direct control of the bleeding if the hemorrhage continues; (*3*) adequate supportive measures, including sedation, antibiotics, and blood transfusions if necessary; (*4*) injection of streptokinase and streptodornase when active bleeding has stopped. A patient with spontaneous hemopneumothorax was successfully treated with multiple aspirations and the use of streptokinase and streptodornase. In this patient, 100,000 units of streptokinase and 25,000 units of streptodornase were injected into the pleural space twenty-one days after the onset of the hemopneumothorax. During the next six days, an additional 250,000 units of streptokinase and 62,500 units of streptodornase were injected in divided doses. Serial chest roentgenograms following thoracentesis showed gradual diminution of the pleural density. Three weeks later films showed almost complete resolution of the hemothorax.—*Spontaneous hemopneumothorax, P. N. Jones & R. S. Bigham, Jr., Ann. Int. Med., October, 1953, 39: 907.*—(*T. H. Noehren*)

**Blood Instillation for Pneumothorax.**—A case of recurrent bilateral spontaneous pneumothorax was successfully treated by instilling blood into the pleural spaces. The ease, simplicity, and effectiveness of this procedure seem to justify its more extensive employment.—*Recurrent bilateral spontaneous pneumothorax treated with artificial hemothorax, L. A. Grossman, Ann. Int. Med., December, 1953, 39: 1303.*—(*T. H. Noehren*)

**Metaplasia of Bronchial Epithelium.**—Squamous metaplasia of bronchial epithelium frequently accompanies pathologic processes, such as measles, diphtheria, pertussis, and influenza. The metaplastic tissue arises from the undifferentiated basal cells of the bron-

chus, which are pluripotential with a capacity for neoplastic growth. To determine the relationship of bronchial epithelial metaplasia and pulmonary neoplasm, the incidence of metaplasia was correlated with anatomic location, age, sex, chronic pulmonary inflammation, and primary lung cancer. From each of 128 unselected autopsies of persons ranging in age from newborn to eighty-six years, 21 representative sections of the trachea and the large and small bronchi were dissected for study. "Squamous metaplasia" was defined as a change to stratified squamous epithelium, and "transitional metaplasia" was defined as a change to stratified epithelium consisting of slightly irregular cuboidal and occasional low columnar cells four to seven layers thick, with no intercellular bridges. When active growth characteristics were present, the squamous or transitional metaplasia was "proliferative." If this growth activity was absent, the metaplasia was "dormant." Of the 128 autopsies, 41 (32 per cent) revealed metaplastic epithelium. Of these cases, 16 were squamous and 25 transitional. Cellular activity was almost equally divided between proliferative and dormant. In the 16 cases of squamous metaplasia, 12 (75 per cent) were proliferative; in the 25 cases of transitional metaplasia, only 36 per cent were of this more rapid-growing type. Apparently, atypical proliferative activity was more common in true squamous metaplasia than in transitional metaplasia. There was no great variation in the incidence of squamous metaplasia between different age groups. The highest incidence of metaplasia (71 per cent) was found in patients with primary lung carcinoma. The next highest incidence was in patients with chronic inflammatory lung disease. The incidence in males was 36 per cent as compared with 20 per cent in females. In no instance was epithelium undergoing neoplastic change. —*Metaplasia of bronchial epithelium: A postmortem study, R. W. Weller, Am. J. Clin. Path., August, 1953, 23: 768.*—(*J. S. Woolley*)

**Bronchial Adenoma.**—Frequently a bronchial adenoma is not suspected until the patient has a roentgenogram. The presence of atelectasis usually suggests the correct diagnosis, and the obstructing lesion is investigated by means of laminagraphy, bronchography, and bronchoscopy. Most of these lesions occur in the larger and main bronchi; biopsy through the bronchoscope is readily obtained; and a specific diagnosis is soon made. Many recent articles emphasize the locally malignant nature and the rare distant metastases of bronchial adenomas. The tumor could arise from mucosal epithelium or from bronchial buds with mesodermal and endodermal elements. The lesion is either carcinoid or cylindromatous. The carcinoid type occurs nine times as often as the cylindromatous type, which is three times as likely to metastasize. Ten per cent of all bronchial adenomas metastasize to a regional lymph node, which is the most frequent site, or to distant organs (liver, lungs, pleura, mediastinum, bone). Lobectomy is the treatment of choice or, when that is not feasible, pneumonectomy. A bronchial adenoma was removed bronchoscopically from a boy four years old, one of the youngest patients reported. The tumor recurred and was resected by pneumonectomy. The adenoma had extended into the peribronchial area and replaced the lymphoid structure within a hilar lymph node. Two years after pneumonectomy, the child was clinically well.—*Bronchial adenoma, S. M. Berger, A. G. Boreadis, & V. Kremens, J. Pediat., October, 1953, 43: 417.*—(*M. J. Small*)

**Bronchial Carcinoma.**—The crude annual death rate from lung cancer in England and Wales has risen from 8 per million persons in 1950 to 278 per million persons in 1952. Among men 28 per cent more deaths were due to bronchogenic carcinoma than cancer of the stomach and more than twice as many as were due to cancer of the colon. Lung cancer accounts for 10 per cent of male deaths between ages of 45 to 54. Only a small part of this increase can be attributed to the increasing proportion of the population living to the cancer age or to improved

diagnostic methods. The incidence of lung cancer is different in various parts of the world, but every country recording vital statistics of lung or respiratory cancer reports a substantial increase in the death rate from bronchogenic carcinoma. Most cases occur in urban centers; in 1950 the death rate from bronchogenic carcinoma was twice as high among male inhabitants of greater London as among men in rural areas. Rates among women showed similar trends. One factor may be atmospheric pollution with waste products in chimney smoke, the exhaust fumes of vehicles, and dust from tarred roads. Among occupational factors, bronchogenic carcinoma may result from prolonged exposure to such atmospheric carcinogens as radon, benzpyrene, and arsenic. These substances are present in town air but in lower concentrations than occur in industry. There is a much higher incidence of lung cancer in men than in women, in the United Kingdom the true ratio being approximately 6 or 7 to 1, and in all countries, the higher the incidence of the disease, the greater the male preponderance. Investigations using various techniques in four countries suggest that tobacco smoking may cause bronchogenic carcinoma. Pipe-smoking, with one exception, has been less closely associated with bronchial carcinoma than cigarette smoking. Users of cigarette holders and filter-tipped cigarettes have been less frequent among lung carcinoma patients than among patients with other diseases, and these devices may remove the active agent before it reaches the respiratory tract. The length of the latent period before the tobacco factor exerts its effect is not known. The higher urban mortality from bronchogenic carcinoma may be explicable on the grounds that cigarette smoking is heavier is these areas. Arsenic may not be the responsible agent since there is a high prevalence of bronchogenic carcinoma in Istanbul, although Turkish tobacco contains little if any arsenic. There is no evidence to implicate exhaust fumes from cars or road dust as carcinogenic agents.—*Bronchial carcinoma: Incidence and aetiology, R. Doll, Brit. M. J., September 5, 1953, No. 4835: 521; and September 12, 1953, No. 4836: 585.*—(*E. A. Riley*)

**Cylindroma of the Trachea.**—The presenting symptoms of cylindroma of the trachea are usually dyspnea caused by a valvular type of obstruction, cough, wheezing or stridor, hemoptysis and hoarseness. Many tracheal cylindromas are diagnosed as asthma. These tumors grow slowly, are highly invasive and recurrent, and can produce metastases. The tumors may be treated by surgical resection, roentgen or radium therapy or both. Metastatic involvement of the lungs is frequent.—*Cylindromas of the trachea, P. L. Clark, O. T. Clagett, & J. R. McDonald, Proc. Staff Meet., Mayo Clin., September 23, 1953, 26: 513.*—(*E. A. Riley*)

**Pulmonary Hamartoma.**—"Hamartoma" is a tumor-like malformation in which the normal components of an organ are abnormally combined. There may be a change of quantity, arrangement or degree of differentiation, or all three. Lesions previously called chondromas of the lung are in reality hamartomas. The tumor may be less than 1 cm. in diameter or massive. In one case the hamartoma occupied all of the right upper lobe of the lung. The usual pulmonary hamartoma is several centimeters in diameter, is generally spheroid, and may be lobulated. It is usually sharply circumscribed and well demarcated, with no surrounding infiltrate. Calcification and sometimes ossification may occur within the lesion. One of the characteristic features is indolence, and a hamartoma generally does not change in size or shape during a period of years. When a hamartoma arises from the inner wall of a bronchus, obstructive emphysema may appear, followed by atelectasis and areas of obstructive pneumonitis. The differential diagnosis is that of any solitary, spheroid, circumscribed pulmonary density, and usually thoracotomy with biopsy must provide a diagnosis.—*Pulmonary hamartoma, J. Stein, H. G. Jacobson, M. H. Poppel, & L. R.*

*Lawrence, Am J. Roentgenol., December, 1953, 70: 971.—(T. H. Noehren)*

**Solitary Circumscribed Lesions.**—A review was made of 156 cases of solitary circumscribed lesions of the lung in which the mass was completely excised surgically. The pathologic finding was malignant neoplasm in 55 cases; this included 12 cases of bronchial adenoma and 17 cases of metastatic lesions. Benign neoplasms were found in 30 cases. Inflammatory lesions were present in 67 cases; 65 of them were granulomas. Four lesions were bronchial cysts. Of the 65 granulomas, 53 were examined bacteriologically. *Coccidioides immitis* was isolated in 3, tubercle bacilli in 7 cases, and *Brucella suis* in one case; no pathologic organism was found in the remaining cases. Two lesions showed the histologic picture of a lipoid granuloma, in one case due to liquid petrolatum; in the other one due to oil from an endogenous source. Patients with bronchogenic carcinoma were most likely to complain of symptoms. In 19 cases there was a previous history of nonpulmonary malignant disease; in 2 cases the pulmonary shadow was caused by a mass which was totally unrelated to the previously excised growth. Among the patients with bronchogenic carcinomas, 74 per cent of those in whom the sedimentation rate was measured had increased values. The information gained from bronchoscopic examination and biopsy was so meager that the wisdom of subjecting all patients with circumscribed lesions to routine bronchoscopic examination is seriously questioned. No bronchogenic carcinoma was found which measured less than 2 cm. in diameter, although several of the metastatic lesions were small. Evidence of calcification constituted the only roentgenographic assurance of benignancy. The postoperative mortality was 1.3 per cent; postoperative complications requiring treatment occurred in 9 patients.—*Solitary circumscribed lesions of the lung: Study of 156 cases in which resection was performed, R. T. Hood, C. A. Good, O. T. Clagett, & J. R. McDonald, J.A.M.A., July 25, 1953, 152: 1185.—(H. Abeles)*

**Meigs' Syndrome.**—A bilateral hydrothorax in a 55-year-old woman was mistaken for several months for an exudative pleurisy and was treated with 23 chest taps before a voluminous ovarian fibroma was detected. The surgical removal of a tumor, the size of an infant's head, from the right ovary was followed by the prompt resorption of the residual pleural fluid. The scant fluid found in the peritoneal cavity during the operation had not previously been detected clinically.—*Zur Kenntnis des Meigs-Syndroms, J. Zimmermann, Deutsche med. Wchnschr., May 29, 1953, 22: 812.—(L. Molnar)*

**Metastases from Breast Cancer.**—A series of 61 patients with pleural or lung metastasis secondary to breast carcinoma were treated with estrogens, and the results compared with those in 66 similar patients who were not treated. In the treated group, 31 per cent of the patients survived longer than twelve months, compared with only 7.5 per cent in the untreated group. In the treated group, 26 per cent of the cases showed regression of pulmonary lesions, compared with none in the untreated group. The effect of estrogens in the cases was temporary, and no prophylactic effect against the development of pulmonary metastases could be shown.—*Treatment by estrogens of pulmonary metastases from breast cancer, B. A. Stoll & F. Ellis, Brit. M. J., October 10, 1953, No. 4840: 796.—(E. A. Riley)*

**Hiatus Hernia and Pregnancy.**—In 9 cases of hiatus hernia diagnosed during pregnancy, the patients' complaints of heartburn and vomiting had mistakenly been ascribed to either functional neurosis or the pregnancy.—*Hiatus and pregnancy, W. A. W. Dutton & H. J. Bland, Brit. M. J. October 17, 1953, No. 4841: 864.—(E. A. Riley)*

**Simultaneous Tomography.**—Theoretically, one roentgenographic exposure can provide pictures of several tissue layers if film sheets are arranged parallel and at the proper

distances. This idea, first described by Manoel de Abreu in 1947, was called "simultaneous tomography." "Monoexpositional stratigraphy" or "pluristratigraphy" might be better names. The author, to get more economical use from roentgen tubes, constructed a simple wooden casette which could be used without changing the roentgenographic apparatus. To photograph three strata of the lung, the most dorsal being at a depth of 10 cm., the films were separated 1.13 cm. For three strata with the most dorsal at 25 cm., the films were separated 1.27 cm. For practical purposes, a standard inter-film distance of 1.2 cm. photographed strata 1 cm. apart in the lung; 0.6 cm. between films showed strata 0.5 cm. apart; and 0.3 cm. gave strata 0.25 cm. apart. The casette was simple to use but it presented other difficulties. Materials inserted between the films absorb roentgen rays, and the intensity of the radiation decreases with the square of distance from the source. Therefore, the third film was regularly underexposed and the picture was not clear. This defect was partially corrected by using the most sensitive film in the third place and by using homogeneous material between films. Compared with standard tomography, the method saves roentgen tubes, technicians are less exposed to radiation, results are more reliable and less dependent on patient cooperation, and pathologic changes are more precisely located or measured.—*Tomography with one exposure (monoexpositional stratigraphy) (Czech), L. Furý, Lék. listy, November 1, 1953, 8: 490.—(J. Ilavsky)*

## ANTIMICROBIAL THERAPY

**Chemotherapy of Tuberculosis.**—As part of a clinical trial of isoniazid (isonicotinic acid hydrazide) in the treatment of pulmonary tuberculosis, 391 patients were studied in 50 hospitals: 119 were treated with streptomycin (1 gm. daily) plus isoniazid (100 mg. twice a day), 100 with streptomycin (1 gm. twice a week) plus isoniazid (100 mg. twice a day), 101 with *p*-aminosalicylic acid (PAS) (sodium salt 5 gm. four times a day) plus isoniazid (100 mg. twice a day), and 71 with PAS (sodium salt 5 gm. twice a day) plus isoniazid (100 mg. twice a day). When submitting a case, the physician did not know which treatment the patient would receive, this being determined by random allocation. The present report analyzes results at the end of three months' treatment. Three main groups were observed: *Group 1*, acute rapidly progressive disease of recent origin; *Group 2*, other forms considered suitable for chemotherapy; *Group 3*, chronic disease considered unlikely to respond to chemotherapy. The principal comparison in the report is between the patients in *Groups 1* and *2* on streptomycin, 1 gm. daily, plus isoniazid, 200 mg. daily (*SH*), and those on PAS (sodium), 20 gm. daily, plus isoniazid, 200 mg. daily (*20 PH*). A full comparison of all four treatments will be made when results for more patients are available. On admission, these two treatment series had a similar distribution of patients with severe and less severe illness. At the end of three months, the general condition had improved in 89 per cent of the *SH* patients and 88 per cent of the *20 PH* patients. The average gain in weight during the period was 12.8 pounds (5.8 kg.) for the *SH* patients and 10.8 pounds (4.9 kg.) for the *20 PH* patients. The temperature fell to normal in 79 per cent of febrile *SH* patients and 85 per cent of febrile *20 PH* patients. In patients with an erythrocyte sedimentation rate of 21 or more before treatment, the rate fell to 10 or less in 37 per cent of those on *SH*, compared with 46 per cent of those on *20 PH*. Changes in radiographic appearances were independently assessed by a radiologist unaware of the treatment of any patient. Two-plus or three-plus improvement was seen in 54 per cent of *SH* and 42 per cent of *20 PH* patients. There were 2 roentgenographic deteriorations and one death on each treatment. None of the above differences is statistically significant. The proportion of patients bacteriologically negative, both on direct examination and on

culture, at a single examination at three months was 65 per cent for the *SH* series and 66 per cent for the *20 PH* series. Bacillary resistance to isoniazid was found in 2 of 39 culture-positive *SH* patients tested at three months, compared with none of 29 similar *20 PH* patients. Bacillary resistance to streptomycin was found in one of 38 culture-positive *SH* patients, and to PAS in one of 28 similar *20 PH* patients. It is concluded, judging solely from the results at three months, that PAS (sodium), 20 gm. daily, plus isoniazid, 200 mg. daily, is a very effective combination of drugs, both clinically and bacteriologically; it ranks with the most efficacious treatment so far studied, namely, streptomycin, 1 gm. daily, plus isoniazid, 200 mg. daily; and streptomycin, 1 gm. daily, plus PAS (sodium), 20 gm. daily. A supplementary clinical comparison of all of the 219 patients on streptomycin plus isoniazid and of all of the 172 on PAS plus isoniazid confirms the clinical efficacy of combining PAS with isoniazid. Patients on streptomycin plus isoniazid gained a little more weight, and a higher proportion showed substantial roentgenographic improvement. A preliminary analysis of results of sensitivity tests on each of the four treatments shows that PAS (sodium), 10 gm. daily, plus isoniazid, 200 mg. daily, may prove to be a bacteriologically effective combination for at least three months. On the other hand, treatment with streptomycin, 1 gm. twice a week, plus isoniazid, 200 mg. daily, is apparently less effective than streptomycin, 1 gm. daily, plus isoniazid, 200 mg. daily, in preventing the development of bacterial resistance to isoniazid during a three-month period (Authors' summary).—*Isoniazid in combination with streptomycin or with PAS in the treatment of pulmonary tuberculosis: A Medical Research Council investigation, Brit. M. J., November 7, 1953, No. 4844: 1005.*—(*E. A. Riley*)

**Intravenous and Rectal Isoniazid.**—The results of isoniazid administered intravenously and in suppositories were compared with the results of oral isoniazid. To date, 1,500 infusions of isoniazid alone and 2,500 infusions of isoniazid plus *p*-aminosalicylic acid (PAS) have been given. Daily doses of isoniazid were 250 to 500 mg., with or without 15 gm. of PAS. Infusions were given for a period of three months, daily during the first month, every other day during the second month, and every two or three days during the third month. Suppositories were given in the same dosage. Blood concentrations, determined by the method of Kelly and Poet slightly modified, were identical whether isoniazid was administered alone or in combination with PAS. The peak blood concentrations obtained after infusion reached 36.8 γ per ml. during infusions of 500 mg. and 31 γ per ml. during infusions of 250 mg. Twenty-four hours after the start of infusion the concentrations were 12 γ with a dose of 500 mg. and 6 γ with a dose of 250 mg. Suppositories produced the same blood concentrations as isoniazid orally. Isoniazid by infusion was generally well tolerated; some gastrointestinal side effects were attributed to PAS. Of 15 patients treated with infusions of isoniazid alone, 12 had recent disease, moderately severe in 7 and severe in 5. Clinically, the results were superior to those reported in a comprehensive study of Paris hospitals using oral isoniazid. After three months, 8 of these 12 patients showed considerable roentgenologic improvement. Of 38 patients treated with isoniazid and PAS intravenously, 26 had recent tuberculosis; 16 showed marked improvement on the roentgenogram after three months. Of 20 moderately large or large cavities, 3 disappeared completely, 6 developed into residual round foci, and 4 decreased considerably in size. In long-standing tuberculosis the same results were obtained as with oral administration. Among 22 patients treated with isoniazid suppositories, 10 of 14 with recent disease improved notably, 5 markedly. Of 7 cavities, 3 disappeared completely. Gastric concentrates were negative in 80 per cent after three months' treatment for recent disease and in 33 per cent of older cases. In the group receiving infusions of isoniazid

alone, one of 6 patients was resistant to isoniazid; after two months, all 3 available strains were resistant; after three months, all 4 available strains were resistant. Intravenous isoniazid alone is thus particularly apt to produce resistance promptly. Infusions of isoniazid and PAS produced resistant strains in 16 per cent of the patients after one month, the same incidence as with oral isoniazid alone. After two months the incidence was 26 per cent for oral isoniazid alone and 30 per cent with infusions of isoniazid and PAS; after three months the incidence of resistance was 50 per cent with intravenous administration and 69 per cent with oral isoniazid. Infusions of isoniazid with PAS gave results better than those with oral isoniazid and should be used as a "treatment of attack" for two months. This leaves streptomycin in reserve to cover possible surgical intervention. —*Étude comparative des divers modes d'administration de l'isoniazide, Pierre-Bourgeois, G. Valette, Vic-Dupont, Mme. Dubois-Verlière, A. Roy, R. Delmas, & J. Savel, Rev. de la tuberc., 1953, 17: 901.*—(*V. Leites*)

**Convulsant Effects of Isoniazid.**—The convulsant effects of isoniazid were studied in a mental hospital. Hydrazides lower the threshold for photic stimulation in both animals and man. Isoniazid alone or in combination with photic stimulation may result in a grand mal seizure when large single intramuscular doses are given. No dosage level of isoniazid up to 45 mg. per Kg. would consistently produce convulsion. A tachycardia of 130 or more occurred in a significant number of patients on high dosage. Iproniazid in a dosage of 15 mg. per Kg. thrice weekly produced severe postural hypotension within three weeks in all patients, whereas single large doses were well tolerated. Iproniazid does not lower the threshold for photic stimulation. The slight change in mental status of some of the schizophrenic patients during hydrazide therapy was not remarkable. —*Convulsant effects of isoniazid, R. H. Reilly, K. F. Killam, E. H. Jenney, W. H. Marshall, T. Tausig, N. S. Apter, & C. C. Pfeiffer, J.A.M.A., August 1, 1953, 152: 1317.*—(*H Abeles*)

**Psychosis Following Isoniazid.**—Tuberculous peritonitis and genitourinary tuberculosis in a 35-year-old woman was treated with isoniazid, 200 mg. thrice daily for three months. Immediately after the cessation of the treatment, she developed psychomotor excitation, edema of the legs, swelling of the face, paresthesias, dryness in the mouth, and urinary retention. About eight days after the beginning of the symptomatology, the patient became violent and had to be hospitalized. These phenomena subsided completely in eight weeks. The severe tuberculous involvement of one kidney may have interfered with the elimination of the isoniazid, and the symptoms observed may have been due to the cumulative effect of the drug.—*Uber akute Psychosen nach Isonikotinsäurehydrazid-Behandlung, K. Conrad & E. Schreib, Deutsche med. Wchnschr., April 17, 1953, 16: 604.*—(*L. Molnar*)

**Isoniazid in Diabetes.**—The effects of isoniazid on carbohydrate metabolism were observed in 9 male and 6 female tuberculous patients with diabetes. Their ages ranged from twenty to fifty-four years, all had moderately severe or severe diabetes requiring insulin, and most had positive sputum. In the beginning, 10 to 15 mg. per kg. were given, and later 5 to 10 mg. per kg., for a total of 30 to 117 gm. in twelve to twenty-five weeks. Improved carbohydrate tolerance was noted in only one case where it might have been a direct effect of the drug on the carbohydrate metabolism. The improved tolerance for carbohydrates in most other cases was compatible with the therapeutic effect of the isoniazid on the tuberculous process. The carbohydrate metabolism was adversely influenced in 5 patients, all of whom had symptoms of intolerance, such as anorexia and flatulence, followed later by jaundice. In 3 of these cases, the resumption of the isoniazid administration, after the disappearance of the signs of hepatic insufficiency, was followed by the

same symptomatology and by impaired carbohydrate tolerance. It is likely that these phenomena were caused by toxic liver damage. The clinical and roentgenographic improvement of the tuberculous process was in general satisfactory, and the careful use of isoniazid is recommended for the treatment of tuberculosis complicated by diabetes, in spite of possible side effects.—*Neoteben-Therapie bei tuberkulösen Diabetikern, H. Scheffler & H. A. Heinsen, Deutsche med. Wchnschr., April 17, 1953, 16: 590.—(L. Molnar)*

**Current Antituberculous Therapy.**—Recent copperative studies, carefully conducted with controls assigned by randomization, have demonstrated that a regimen of 1 gm. of streptomycin twice a week and 12 gm. of *p*-aminosalicylic acid (PAS) daily for periods up to one year has great therapeutic efficacy and relatively little toxicity or drug resistance. Isoniazid in combination with streptomycin or with PAS appears to be effective, although there has not been time for as complete an evaluation as with streptomycin and PAS. Chemotherapy generally is less satisfactory when there has been prior chemotherapy, in part because of drug resistance. When partial streptomycin resistance has developed, continued administration of streptomycin has some value unless resistance becomes complete to 100 γ per ml. Isoniazid, as a second effective drug, improves the clinical outlook for such patients. When drug resistance to both streptomycin and isoniazid has developed, viomycin is effective, although probably less so than streptomycin or isoniazid. Combined therapy with more than one antituberculous drug is always desirable, and PAS appears best to give with either streptomycin or isoniazid. When intolerance to PAS exists, oxytetracycline may be used. Effective chemotherapy resolves the reversible components of the disease in most cases, leaving residual fibrosis and necrosis. The best clinical management of such residual tuberculous disease has not yet been determined.—*Current status of chemotherapy, W. B. Tucker, Ann. Int. Med., November, 1953, 39: 1045.—(T. H. Noehren)*

**Treatment of Tuberculous Meningitis.**—The results of treating Negro children with tuberculous meningitis were compared with the results obtained in white children treated in the same manner. Between October, 1947, and January, 1953, 34 Negro and 6 white children were admitted with tuberculous meningitis. Usually, intramuscular streptomycin or dihydrostreptomycin, 20 to 40 mg. per pound of body weight, was given for a six-month period; forty injections of intrathecal streptomycin, 25 to 100 mg. each, were used for a period of nine weeks or less. Recently, intrathecal streptomycin therapy has been decreased or completely eliminated. Sufficient Promizole was given to maintain a blood concentration of 1 to 3 mg. per 100 ml., but recently *p*-aminosalicylic acid (PAS) has replaced Promizole. In the last 7 cases, isoniazid 4 mg. per kg. of body weight per day, later increased to 8 mg., was used; if possible, for approximately six months. Two moribund patients received intrathecal PPD as suggested by Cairns, Smith, and Vollum. One patient died, but the other improved markedly and his cerebrospinal fluid is now normal. Of the 40 patients, 18 (45 per cent) are alive at least six months after treatment was begun; 13 are Negroes and 5 are white. Of the survivors, 8 have lived longer than three years, and one is apparently well after five and one-half years. The survival rate among the 34 Negro children is 38 per cent, while the survival rate of the 6 white patients is 83 per cent. Of the 28 Negro and 5 white patients who did not have isoniazid, 14 (42 per cent) have survived longer than six months. Of 6 Negroes and one white patient who received isoniazid in addition to streptomycin and PAS, 4 (57 per cent) have lived longer than six months. One of those who died was progressing satisfactorily until he fractured his skull during a manic spell, presumably as a result of isoniazid therapy. The other patient who died first received isoniazid late in his disease. Miliary tu-

berculosis was also present in 13 patients, of whom only 4 survived. Of the 27 patients who did not have demonstrable miliary tuberculosis, 14 are living. Of 3 patients who had miliary tuberculosis in addition to tuberculous meningitis and were treated with isoniazid, 2 are alive six months later.—*The treatment of tuberculous meningitis in children, E. L. Kendig, Jr., R. Ownby, Jr., G. E. Trevathan, & L. E. Sutton, Jr., J. Pediat., November, 1953, 43: 532.*—(*M. J. Small*)

**Streptomycin-Treated Renal Tuberculosis.**—To study the effect of streptomycin on chronic renal tuberculosis, the lesions in 37 specimens from patients without specific drug treatment were compared with those in 9 specimens from patients treated with streptomycin alone, 1 gm. daily for ninety days, and with those in 4 specimens from patients treated with streptomycin plus *p*-aminosalicylic acid (PAS), 1 gm. of streptomycin and 20 gm. of PAS daily for 90 days. Of the specimens without specific drug treatment, 83.3 per cent showed acute caseating tuberculous granulation tissue in "open" cavity walls and all showed acute lesions in the mucosa of calyx, pelvis, or ureter. Lesions due to secondary pyogenic infection were found in 34 of the 37 specimens. Specimens from the 9 patients treated with streptomycin alone showed fibrosis greater than was found in corresponding lesions in the untreated patients. Lesions in the mucosa of calyx, pelvis, or ureter showed less fibrosis than in other areas, largely because of the development of streptomycin-resistant strains of tubercle bacilli, indicating that the treatment with streptomycin alone was not satisfactory in some of the cases. Reactivation of tuberculous lesions might also have resulted from secondary pyogenic infection. Tuberculous lesions in the specimens of 4 patients who had been treated with streptomycin and PAS showed as much more fibrosis than after streptomycin alone as the latter did when compared with the untreated specimens. Secondary pyogenic infection was not acute in any of the streptomycin-PAS specimens.—*The effects of streptomycin, with and without para-aminosalicylic acid, on the pathological histology of renal tuberculosis, J. C. Dick, J. Path. & Bact., October, 1953, 66: 365.*—(*H. J. Henderson*)

**Intravenous Streptomycin.**—One hundred patients with pulmonary tuberculosis were treated with daily streptomycin by intravenous infusions lasting three hours. Streptomycin was always used with *p*-aminosalicylic acid (PAS) and administered in three ways: (*1*) streptomycin dissolved in a 3 per cent PAS solution for intravenous infusion, using a dilution of 0.5 gm. per liter for the first infusions followed by 1 gm. of streptomycin per 500 ml. (95 patients); (*2*) streptomycin dissolved in saline, 1 gm. per 500 ml., with PAS orally (5 patients); and (*3*) the last 1,300 infusions contained 250 mg. of isoniazid in addition to streptomycin and PAS. Treatment continued for 30 to 148 days, averaging 50 days. The pH of the solution was 6.9 for 3 per cent PAS, 5.4 for 10 per cent streptomycin in distilled water, and 6.6 for 1 per cent streptomycin in 3 per cent PAS solution. Thus the pH of streptomycin and PAS solution is more favorable than that of streptomycin in 10 per cent solution as for intramuscular injection. Intravenous streptomycin produced no intolerance. The only reactions were rare cases of headache and sensations of heat like those observed with PAS alone. Among 40 patients, 12 had a moderate increase in the eosinophil count, up to 10 per cent. No vestibular or auditory disturbances were noted. There was one cutaneous reaction which recurred after intramuscular administration. In 34 patients sputum conversion was so rapid that sensitivity studies were not feasible. In 6 patients the susceptibility to streptomycin and PAS was unaffected after 60 to 100 days of treatment. In 6 patients who received streptomycin, PAS, and isoniazid intravenously, susceptibility was maintained after an average of 50 infusions. In 80 per cent of the patients, there was sputum conversion on culture. Recent cavitary-nodular tuberculosis showed spectacular roentgenographic improvement in 50 per cent,

considerable improvement in 43 per cent, and slight improvement in 7 per cent. Older nodular and cavitary lesions showed spectacular improvement in 18 per cent, marked improvement in 46 per cent, and slight improvement in 36 per cent. Old far advanced, extensive cavitary lesions showed no spectacular improvement, marked improvement in 33 per cent, slight improvement in 50 per cent, and no improvement in 17 per cent. Several cases of progressive primary tuberculosis, one case of miliary tuberculosis, 3 cases of tuberculous meningitis, and one case of genitourinary tuberculosis were also successfully treated.—*Streptomycine en perfusion veineuse: Résultats de cent cures et de cinq mille perfusions, Y. Hébraud, M. Bertrac, & P. Maufoy, Presse méd., October, 1953, 61: 1269.*—(*V. Leites*)

**Treatment of Blastomycosis.**—Three patients with proved systemic North American blastomycosis and one case of the cutaneous form of this disease were successfully treated with 2-hydroxystilbamidine. Extensive clinical and laboratory studies revealed no definite evidence of toxicity resulting from the prolonged and extensive administration of 2-hydroxystilbamidine. In none of the cases did trigeminal neuropathy develop. *In vitro* studies established a definite inhibitory effect of 2-hydroxystilbamidine on four strains of *B. dermatitidis*; 2-hydroxystilbamidine may be slightly more effective than stilbamidine on the mold phase of this organism. In critical cases of systemic North American blastomycosis, chlortetracycline may advantageously be combined with 2-hydrostilbamidine in treatment (Author's summary).—*Treatment of blastomycosis, I. Snapper & L. V. McVay, Jr., Am. J. Med., November, 1953, 15: 603.*—(*T. H. Nochren*)

**Erythromycin for Pneumococcal Pneumonia.**—Of 50 patients with pneumococcal lobar pneumonia, 24 were treated with erythromycin and 26 with penicillin. The results with these 2 agents were similar in regard to duration of fever, duration of leukocytosis, complications, and deaths. Erythromycin acts against a limited number of bacterial species and should be used only when the bacteriologic diagnosis can be made. Some bacterial species, including the pneumococcus, may develop *in vitro* a clinically significant degree of resistance to erythromycin. Erythromycin is relatively insoluble and there was no parenteral preparation at the time of this study. It thus seemed less suitable than penicillin for treating critically ill patients who might require immediately adequate blood and tissue levels of an antibacterial agent. For these reasons, erythromycin should be reserved as an alternative therapy for pneumococcal lobar pneumonia, its principal value being that it may be administered to patients who are hypersensitive to penicillin.—*The relative efficacy of erythromycin (Ilotycin) and of penicillin in the treatment of pneumococcal lobar pneumonia, R. Austrian & R. Rosenblum, Am. J. M. Sc., November, 1953, 226: 487.*—(*W. J. Steininger*)

**Chlortetracycline and Atypical Pneumonia.**—In a controlled study of 212 patients from a single epidemic of primary atypical pneumonia, the effects of chlortetracycline (Aureomycin) were compared with the effects of chlortetracycline-simulated placebos in severely ill patients, patients with radiologic evidence of pneumonia only, and in all patients of the series. Evaluation of the duration of the major symptom, fever, of the physical and radiologic signs of disease, and of the incidence of progression, relapse, and marked remission within forty-eight hours of the initiation of therapy indicated that chlortetracycline does not influence the course of this disease (Author's summary).—*Aureomycin in atypical pneumonia, S. H. Walker, Am. J. Med., November, 1953, 15: 593.*—(*T. H. Nochren*)

**Subphrenic Abscess.**—A 42-year-old man developed a subphrenic abscess following cholecystectomy and choledochostomy. Treatment with intravenous oxytetracycline resulted in complete recovery without surgical

interference.—*Cure of subphrenic abscess with large doses of oxytetracycline (Terramycin), J. Zaslow & F. Sachs, J.A.M.A., July 25, 1953, **152:** 1213.—(H. Abeles)*

**Chlortetracycline in Congestive Failure.**—In an attempt to reduce the incidence of intercurrent respiratory infections, 149 cases of chronic congestive failure were observed for an average of twenty months. To 73 of this group, 500 mg. of chlortetracycline was administered daily; the other 76 were controls. The administration of chlortetracycline diminished the incidence of infection and increased the appetite, strength, and sense of well-being. Evident toxic effects were minimal although these patients were subjected to comprehensive clinical and laboratory examinations. While additional observations are necessary, it appears that prolonged antibiotic prophylactic therapy is of value in chronic congestive failure.—*Antibiotic prophylaxis in chronic congestive failure, L. V. McVay, Jr., D. H. Sprunt, & T. N. Stern, Am. J. M. Sc., November, 1953, **226:** 491.—(W. J. Steininger)*

**Metabolism of Izoniazid.**—Six *Rhesus* monkeys were used in an excretion study to determine the metabolic fate of isoniazid. The equivalent of more than 50 per cent of the isoniazid administered was excreted in the urine. The solubility properties showed that the crystalline material isolated from monkey urine was 1-isonicotinyl-2-acetylhydrazine. The acetyl derivative accounted for 78 to 94 per cent of the isoniazid-like materials eliminated by the various monkeys and 91 per cent of that excreted by a human subject. Acetylation of isoniazid is probably significant insofar as the toxicity and chemotherapeutic activity of this hydrazine is concerned. Variations in the completeness of acetylation might well account for the relatively great differences in the toxicity of isoniazid for different patients. The greater the acetylation, the less the toxicity. From the chemotherapeutic viewpoint, however, acetylation of isoniazid is undesirable, for, as with acetylation of the sulfonamides, the process leads to a striking loss in chemotherapeutic activity. In view of this, a search for isoniazid derivatives less susceptible to acetylation or for selective methods of blocking the acetylation process might discover compounds with greater *in vivo* activity against infections with tubercle bacilli or more effective methods of treating such infections with isoniazid per se.—*On the metabolic fate of isoniazid, H. B. Hughes, J. Pharmacol. & Exper. Therap., December, 1953, **109:** 444.—(E. Dunner)*

**Catalase of Tubercle Bacilli.**—A study was started on the assumption that a chemotherapeutic agent is active through its effect upon the enzymatic system of pathogenic microorganisms. The activity of *p*-aminosalicylic acid and isoniazid upon the catalase of a *Mycobacterium tuberculosis* suspension was studied. Neither of these agents seemed to have any substantial effect.—*Qualitative studies of catalase in tubercle bacilli (Czech), M. Polster, Lék listy, December 1, 1953, **8:** 354.—(J. Ilavsky)*

**Bacterial Resistance to Isoniazid.**—Tubercle bacilli from 80 cases of pulmonary tuberculosis treated with isoniazid alone in various sanatoriums were tested for isoniazid resistance. Some patients had earlier received other treatment. Using the American Trudeau Society solid medium, each specimen was tested at least against 0.1, 0.5, and 5 γ of isoniazid per ml. The suspensions of tubercle bacilli were homogenized with soda, neutralized, treated with malachite green, and centrifuged before resuspension in physiologic solution. The surface of the medium was examined after two weeks' incubation and then every week for eight weeks. Sputum from every case was tested each week during the first four months of the study, then each month for the remainder of the treatment, and again at its close. Altogether more than 1,200 direct tests were made. In 54 of 55 cases tested, tubercle bacilli were initially susceptible to 0.5 γ of isoniazid per ml. During treatment, 47 cases were tested regularly; 14

became permanently resistant, 18 temporarily so, and 15 remained susceptible. Resistance to 5 γ per ml. was attained in 70 per cent of the cases between the third and fourth weeks of the treatment. This resistance appeared suddenly in half of the cases and progressively in one-third. Resistance to 50 γ per ml. never appeared. In one-third of the cases followed after treatment, resistance to isoniazid gradually diminished but never disappeared. Of 14 patients whose sputum had never before contained acid-fast bacilli, 11 expectorated tubercle bacilli resistant to 0.5 γ of isoniazid per ml. until the sixth to the eleventh weeks of treatment. Three were still negative thirteen to seventeen weeks after treatment was begun. Isoniazid should not be used alone to the exclusion of other measures. —*Contribution à l'étude de la resistance à l'isonicotinic acid hydrazide, A. Petit, Acta tuberc. belg., October, 1953, 44: 337.*—(*A. T. Laird*)

**Electron Microscopy of Drug Action on Tubercle Bacilli.**—The morphologic changes in different strains of tubercle bacilli were studied by means of an electron microscope after the organisms were exposed to streptomycin, *p*-aminosalicylic acid (PAS), or amithiozone. Bacilli were cultivated on Sauton liquid medium, and antituberculous substances were added to the medium. The size of the bacilli varied. Six-day-old bacilli had the length of 1.5 μ, nine- and twelve-day-old bacilli reached 1.5 to 2.5 μ. In young cells the cell wall was not seen, but it was observed in nine- and twelve-day-old bacilli. The granular bodies were seen arranged along the axis of the bacilli. After six days' exposure to 3 units of streptomycin per ml., the bacilli had swollen and the granular substance was a formless mass. After nine days of contact with streptomycin, loose fibers and granules were all that remained of the bacilli. The bacilli were lysed by 0.1 mg. of PAS per ml. The combined action of streptomycin and PAS was stronger than the action of either compound alone.—*Action of chemotherapeutic compounds on the tubercle bacilli studied in electron microscope (Russian), E. I. Tchertkova & N. I. Buinov, Problemi Tuberkuloza, January-February, 1953, No. 1: 22.*—(*E. Darzins*)

**Isoniazid with Other Drugs.**—The inhibitory effect of such antituberculous agents as streptomycin, *p*-aminosalicylic acid (PAS), and amithiozone is stabilized when they are used in combination with isoniazid. *In vitro* experiments were done in liquid Dubos medium with a ten- to fifteen-day-old strain of *M. tuberculosis* H37Rv. In some 50 titrations, the following were the limits of the inhibitory effect: isoniazid alone, 1 γ per ml.; PAS alone, 22.5 γ per ml.; amithiozone alone, 20 γ per ml.; streptomycin alone, 0.5 γ per ml. The combination of isoniazid and PAS was used in 15 experiments with concentrations of isoniazid from 0.2 per cent to 10 per cent. The mean inhibitory concentration was 0.098 γ of isoniazid, only one-tenth that for isoniazid alone, and 4.3 γ of PAS, only one-fifth that for PAS alone. Combined use of isoniazid and amithiozone gave analogous results *in vitro*, as did isoniazid and streptomycin. The synergism of isoniazid and the other antituberculous drugs was shown in a series of experiments combining a given and insufficient concentration of one of the drugs with a variable but insufficient concentration of isoniazid. The combinations of isoniazid with streptomycin, isoniazid with PAS, and isoniazid with PAS and streptomycin were studied in this manner. The inhibitory concentration of isoniazid was considerably decreased if used in the various combinations. —*Action combinée in vitro de différents tuberculicides avec l'hydrazide de l'acide isonicotinique (INH), Mme. Aïtoff, Ann. Inst. Pasteur, August, 1953, 85: 164.*—(*V. Leites*)

## LABORATORY STUDIES

**Pathogenesis and Pathophysiology of Experimental Tuberculosis.**—Although digestive disturbances, such as the lack of appetite, are common among tuberculous patients, the

causes of these disturbances are little known. The best animal on which to study these problems, according to Pavlov's methods, is the dog. The main advantage of the dog is that it is resistant to tuberculosis. A method of infecting this animal was developed, using intravenously mixed strains of tubercle bacilli isolated from tuberculous patients; neither the size nor the virulence of the inoculum being indicated. In one series of 8 infected dogs, loss of weight, rise of body temperature, and rapid decline of appetite were observed. These animals were infected a second time with larger inocula of bacilli, after which they developed high fever, lost weight, and lived 68 to 142 days. The autopsy showed specific tuberculous lesions in the lungs, spleen, and kidneys. Another group of 4 animals was successively infected three times with tubercle bacilli. One dog died in 128 days, 3 others survived. The chronic course of tuberculosis in dogs made it possible to study by means of conditioned reflexes the influence of higher nervous activity on digestion in these animals after surgical intervention as perfected by Pavlov. The changes in conditioned and non-conditioned salivation reflexes were studied in 7 dogs. In infected animals, the secretion of saliva decreased early. In some of the animals the secretion ceased completely, and the animals refused to eat. The conditioned sight and smell reflexes decreased progressively as the infection progressed. The loss of appetite in tuberculosis is of cortical origin, resulting from decreased stimulation of the digestive center of the cerebral cortex. On the third and fourth days after infection, the secretory function of part of the stomach, isolated according to Pavlov, showed a great increase in volume and a considerable augmentation in the activity of the juice. At the end of the disease the digestive capacity of the juice decreased, and lumps of meat were not digested after even eight hours' exposure to it. The digestive capacity of the intestines decreased too, but the amylolytic activity of the intestinal juice increased during the acute period of the disease. The motility of the stomach and intestines increased as the disease progressed. These observations agree with those on tuberculous patients, showing that increased excitability of the vagal nerve, which regulates the motility of intestines, coincides with aggravation of the disease. The reflex and tonic excitability of the centers of the vagal nerve in the brain is in direct relation to the activity of the brain cortex. The higher nervous functions of 5 tuberculous dogs, including animals with feeble and vigorous higher nervous activity, and the hypnotic conditions of these animals in connection with the activity of the brain were studied, but no details or results are given.—*Some general results of the investigations of the pathogenesis and pathophysiology of experimental tuberculosis* (*Russian*), *G. V. Peshkovsky, Problemi Tuberkuloza, March-April, 1953, No. 2: 52.*—(*E. Darzins*)

**Experimental Tuberculous Meningitis.**—Two different dosages of streptomycin were compared for effectiveness in treating experimental tuberculous meningitis. Guinea pigs were inoculated intrathecally with tubercle bacilli of human type (H37Rv) and fourteen days later divided into three groups of 10 each, namely: (*1*) untreated controls, (*2*) treated with 6 mg. of streptomycin daily, and (*3*) treated with 30 mg. of streptomycin daily. The antibiotic was administered in a single, daily intramuscular dose, and the study was terminated after 192 days. Signs of meningeal dysfunction became evident during the first two weeks of infection in most animals. Complete or partial paralysis of the hind legs and, less frequently, of the forelegs occurred in many animals, but less frequently in the animals which were treated longest. Histologically, there was periventricular degeneration, hydrocephalus, usually of a mild degree, and diffuse leptomeningitis, the latter being particularly evident in animals which died early. After prolonged treatment, especially with the larger doses, healing became manifest; most of the residual lesions were chronic, well-fibrosed, granulomatous reactions. It is concluded that: (*1*) extensive experimental meningeal tuberculosis induced intrathecally in the highly susceptible guinea pig is

amenable to the deterrent influence of streptomycin; (*2*) prolonged antimicrobial therapy is essential for maximal beneficial results; (*3*) in the guinea pig, a dose of 30 mg. of streptomycin daily is more effective than a dose of 6 mg. daily, and (*4*) a more efficient antimicrobial agent is needed to treat tuberculous meningitis.—*Chemotherapy of experimental tuberculous meningitis in guinea pigs: Use of various dosages of streptomycin, R. P. Stevens, A. G. Karlson, & W. H. Feldman, Proc. Staff Meet., Mayo Clin., October 21, 1953, 28: 599.*—(*E. A. Riley*)

**Guinea Pig Inoculation.**—A new method of inoculating guinea pigs prevents mixed infections. An earlier method utilizing penicillin gave remarkable results in 2,272 inoculations. Later results were less satisfactory. At present, sputum or any other pathologic material is mixed with 2 ml. of physiologic saline solution containing 0.01 gm. of chlortetracycline. Ten minutes later the mixture is injected subcutaneously. In contrast to penicillin, chlortetracycline is nontoxic for the guinea pig. Comparison of the two methods in two groups of 33 guinea pigs revealed that 4 guinea pigs died in the penicillin group and one in the chlortetracycline group. The tuberculin test, 1:10, was positive in 16 guinea pigs of the penicillin group and 22 of the chlortetracycline group. —*Nouvelle technique d'inoculation au cobaye de produits surinfectés pour la recherche du bacille tuberculeux: Usage de l'auréomycine, F. Tison, Ann. Inst. Pasteur, August, 1953, 85: 274.*—(*V. Leites*)

**Tuberculin and Cortisone Effects on Cells.**—The growth of cells explanted from tuberculin-sensitive animals may be inhibited by tuberculin added to the culture menstrum. Initially, it was planned to observe the effect of cortisone on this tuberculin reaction. Tuberculin and cortisone in themselves had considerable toxicity, however, for cells from normal, infected, and immunized animals. Tuberculin (PPD) and cortisone acetate, singly and in combination, were added to explanted splenic tissue from guinea pigs, mice, and rabbits, and to the buffy coat of rabbit blood. These tissues came from normal animals or from animals which had been infected with tubercle bacilli or immunized with killed tubercle bacilli. No greater concentrations than 5 γ of tuberculin or 0.5 γ of cortisone per ml. were tolerated by cultured cells from normal animals. PPD selectively damaged only the growing cells of splenic tissue from sensitive pigs and, to a lesser degree, the migrating cells of buffy coat obtained from sensitive rabbits. Cortisone was more toxic for explanted splenic cells from tuberculin-sensitive guinea pigs. The specific effect of PPD on tissues from tuberculin-sensitive animals was not modified by cortisone. Thus, these data furnished no evidence that cortisone directly affected the response of sensitive cells to PPD. These results differ from those of other investigators using different techniques, but *in vivo* as well as *in vitro* experiments indicate that the toxic dose of cortisone varies from tissue to tissue in the same species and in different animals.—*The effect of tuberculin and cortisone singly and in combination on explanted tissues of guinea pigs, mice, and rabbits, M. Holden, B. C. Seegal, & L. B. Adams, J. Exper. Med., December 1, 1953, 98: 551.*—(*J. S. Woolley*)

**Blood Media for *M. Tuberculosis*.**—A modified human blood medium containing 50 units of penicillin per ml. was compared with the Löwenstein-Jensen medium. Of 1,012 specimens, 378 were positive. Of these 93.6 per cent were obtained on the blood medium as compared to 89.9 per cent on the Löwenstein-Jensen medium; the difference of 3.7 per cent is not significant. While 38 strains of tubercle bacilli grew on the blood medium but not on the Löwenstein-Jensen medium, 24 strains which grew on the latter medium failed to develop on the former. Growth appeared slightly earlier on the blood medium. There were 5 per cent contaminations on the blood medium and 6.9 per cent on the Löwenstein-Jensen medium. Certain dysgonic mycobacteria grew better on blood than on egg

media. Some strains of *M. tuberculosis* are culturally variable and maximum efficiency is not likely to be achieved with a single medium. The blood medium is very satisfactory for determining the susceptibility of tubercle bacilli to streptomycin and isoniazid. The chief advantages of the blood medium are economy, simplicity of preparation, and ability to grow tubercle bacilli from small inocula easily, recognizably, and in a short time. Refrigerated media are exceedingly stable in tightly sealed screw-cap tubes for as long as four months.—*Blood media for the cultivation of Mycobacterium tuberculosis: VII. Comparison of blood agar-penicillin and Löwenstein-Jensen media under routine diagnostic conditions, M. S. Tarshis, P. A. Kinsella, & M. V. Parker, J. Bact., October, 1953, 66: 448.—(F. G. Petrik)*

**Cultivation of *M. Johnei*.**—Solid and liquid media devised by Dubos for the cultivation of *M. tuberculosis* were modified for *M. johnei*. Dubos solid and liquid media containing *M. phlei* extracts were unable to support the growth of *M. johnei* unless a 20 per cent concentration of inactivated serum was added. Cow, horse, sheep, pig, rabbit, and chicken sera were equally satisfactory and as good as bovine albumin fraction V for the liquid medium or the oleic-acid–albumin complex for the solid medium. Of several extracts of *M. phlei*, an alcoholic one was chosen. This was prepared by growing *M. phlei* on glycerol-agar, removing the growth, heating to 80° C. for thirty minutes, drying in a desiccator, and then grinding to a fine powder. The powder was extracted three times with industrial alcohol under a reflux condenser. The extract was filtered through paper and concentrated by evaporation. To the orange-red viscous fluid which remained, 80 ml. of 50 per cent glycerol in distilled water were added. The pH was adjusted to 7.6, and the solution was heated on a boiling water bath for ten minutes. While hot, it was placed in a separatory funnel overnight; the red oil on the surface was discarded. The remaining, almost clear fluid was adjusted to pH 7.0, autoclaved at 5 pounds of pressure for twenty minutes, and used in the basal media in amounts to give a final concentration equivalent to 0.5 per cent of dried *M. phlei* and 1.0 per cent of glycerol. Penicillin was added, 2 units per ml. of liquid medium and 50 units per ml. of solid medium. Bovine strains of *M. johnei* often grew more rapidly on these media than on Taylor's egg medium, the transparent solid medium allowed growth to be more easily detected, and the added penicillin helped to control contaminants in biologic material.—*Modifications of Dubos's media for the cultivation of Mycobacterium johnei, H. Williams Smith, J. Path. & Bact., October, 1953, 66: 375.—(H. J. Henderson)*

**Tween and Bacillary Growth.**—The effect of Tween 80 on the growth curve of tubercle bacilli was studied by comparing Sauton's medium with or without Tween, using a smooth avian strain, 923 (Paris Pasteur Institute). The addition of Tween to the medium accelerated bacillary growth. The time of bacterial division was twenty-two hours on Sauton alone and fourteen hours on Sauton with 1 per cent Tween. The tubercle bacilli could utilize Tween as the only source of carbohydrate. Growth curves on Sauton containing, as the sole source of carbohydrate, 5 per cent glycerin, and Sauton-Tween with 5 per cent glycerin and 1 per cent Tween, showed that there was no "diauxie." The bacilli utilized simultaneously and probably through different enzymatic systems the 2 sources of carbohydrate. Increased growth on Tween medium can thus be explained without invoking a modification of the permeability of bacilli by the surface active agent.—*Action des agents tensioactifs sur le bacille de Koch: le Tween 80, D. Luzatti, Ann. Inst. Pasteur, August, 1953, 85: 277.—(V. Leites)*

**Fatty Acids from Tubercle Bacilli.**—The fatty acids from the alcohol-ether-soluble lipids of 3 strains of human-type tubercle bacilli were isolated by fractional distillation and chromatography on charcoal. The components were identified by means of the ultra-

violet spectra and the use of urea complexes. Three major components were similar in each lot of acids: 28 to 34 per cent palmitic acid, 32 to 39 per cent $C_{18}$ and $C_{19}$ acids, and 16 to 21 per cent higher molecular weight acids, of which one-third consisted of a $\alpha$-methyl-$\alpha,\beta$-unsaturated acids. Some of the higher molecular weight acids also contained nonconjugated unsaturation. The fraction of $C_{18}$ and $C_{19}$ acids consisted largely of *n*-octadecanoic acid, stearic acid, and tuberculostearic acid. This latter acid was present as such and not formed by hydrogenation of an unsaturated acid or one containing a cyclopropane ring. This supports the idea that tuberculostearic acid is a component of the lipids of the tubercle bacillus.—*Certain characteristics of the fatty acids from the lipides of the tubercle bacillus, James Cason, Gene Sumrell, C. Freeman Allen, George A. Gillies, & Sanford Elberg, J. Biol. Chem., November, 1953, 205: 435.*—(*E. Soto Figueroa*)

**Arithmetic Linear Growth of Mycobacteria.**—Cultures of the BCG strain of *Mycobacterium tuberculosis* var. *bovis*, *M. phlei*, *M. smegmatis*, *Micrococcus lysodeikticus*, and *Sarcina lutea* will grow logarithmically when they are aerated continuously by shaking. Arithmetic linear growth is obtained only when the cultures are not aerated.—*An explanation for the arithmetic linear growth of mycobacteria, W. A. Volk & Q. N. Myrvik, J. Bact., October, 1953, 66: 386.*—(*F. G. Petrik*)

**Catechol Oxidation by *M. Butyricum*.**—Cell-free extracts prepared from *Mycobacterium butyricum* oxidize catechol to $\beta$-ketoadipic acid. Comparison of the rates of catechol disappearance in the presence of intact cells and of extracts indicates that this is the only mechanism for catechol oxidation by *M. butyricum* (Authors' summary).—*The mechanism of catechol oxidation by Mycobacterium butyricum, W. R. Sistrom & R. Y. Stanier, J. Bact., October, 1953, 66: 404.*—(*F. G. Petrik*)

**Toxicity of Silica.**—The equilibrium system of silica gel-silicic acid-water contains between 166 and 170 mg. of silicon dioxide per liter dispersed as silicic acid in the water phase. Silicic acid is rapidly excreted in the urine whether it arises as a result of solution of particulate material or silicate administered parenterally. The rate of solution of quartz particles is depressed by albumin and greatly enhanced by the presence of salts in the solvent water. Albumin in a silicic acid solution inhibits gel formation at concentrations greatly in excess of the equilibrium value found for the silica gel-silicic acid-water system. Thus it is improbable that colloidal silica gel can be formed in the tissue fluids from the solution of particulate silica deposited in the tissues. Because of the lack of demonstrable toxicity obtained with soluble silica, it is necessary to find another explanation for the toxicity of silica in tissues as manifested in the disease silicosis (Author's summary).—*Toxicity of silica, L. D. Scheel, E. Fleisher, & F. W. Klemperer, A. M. A. Arch. Indust. Hyg. & Occup. Med., December, 1953, 8: 564.*—(*T. H. Noehren*)

## PUBLIC HEALTH AND EPIDEMIOLOGY

**Silicosis in Miners in India.**—The problem of free silica exposure and silicosis in mica miners of Bihar, India, was investigated. Medical examinations were made of a representative sample of 329 miners, including chest roentgenograms on 11- by 14-inch films. The chemical nature of the rock dust, as well as the degree of dustiness in the mining operations, was determined. The rock dust to which the miners were exposed varied in silica content from 11 to 67 per cent, with a median of 42 per cent. The degree of dustiness varied from one occupation to another and was highest for pneumatic drilling alone with no dust-control measures, and lowest for wet drilling. Nodular and conglomerate silicosis was found in 34.1 per cent of the miners and was directly associated with the degree of

dustiness of the occupations as well as the duration of time that the miners had worked at these occupations. Pulmonary tuberculosis was found in 18.6 per cent of the miners.—*Silicosis in mica mining in India, H. Heimann, G. S. Moskowitz, C. R. H. Iyer, M. N. Gupta, & N. S. Manikiker, A. M. A. Arch. Indust. Hyg. & Occup. Med., November, 1953, 8: 420.*—(*T. H. Noehren*)

**Pneumoconiosis in Tool Workers.**—Three workers in the tungsten-carbide industry had peculiar pulmonary reactions and hyperglobulinemia. These workers probably manifested a specific reaction to the inhalation of an industrial dust or a combination of dusts. One man improved roentgenographically when removed from the industrial environment; the other 2 remained virtually static during one year's observation. All 3 workers became asymptomatic when removed from exposure to dust. These men were exposed to tungsten carbide, tantalum, titanium, cobalt, silicon carbide, aluminum oxide, and diamond dusts for a period of six to eight years. All but the tungsten carbide, silicon carbide, and cobalt have been generally conceded to be inert and innocuous. Injections of silicon carbide into the peritoneum and lungs of rats produced only a foreign-body reaction like that to any inert dust rather than a specific fibrosing response like that to certain dusts. Silicon carbide could thus be excluded as a causative factor. Each man had a negative tuberculin test, and cobalt seemed the most likely cause of the condition. Powdered cobalt and nickel are known to produce dermatitis characterized by hyperemic, edematous, and vesicular lesions, apparently due to hypersensitivity. Individual susceptibility thus may be an important factor in pulmonary disease. In these tool industry workers, a combination of various powdered metals may have been necessary to produce this reaction in the lung.—*Pneumoconiosis in a tool industry, C. W. Miller, M. W. Davis, A. Goldman, & J. P. Wyatt, A. M. A. Arch. Indust. Hyg. & Occup. Med., November, 1953, 8: 453.*—(*T. H. Noehren*)

**Asbestosis and Cancer.**—Asbestosis, caused by the occupational inhalation of asbestos fibers, leads to progressive fibrosis and scarring within the lungs. The pathologic processes are believed not to be due to the chemical nature of asbestos particles; rather, the mechanical irritation from fibers lodged in the respiratory bronchioles initiates a foreign-body reaction which eventually leads to fibrosis. The pathologic events occur in three stages: (*1*) desquamation and exudation, (*2*) formation of asbestosis bodies, and (*3*) fibrosis and scarring. In general, five to seven years elapse between the initial exposure to high concentrations of the asbestos dusts and the onset of clinical asbestosis. While most patients with asbestosis have had an exposure of ten to sixteen years, the disease has occurred with as brief an industrial exposure as six months. Usually symptoms appear only when the respiratory reserve has been greatly reduced by the fibrosis. When the symptoms once begin and significant dyspnea appears, progression is usually definite and rapid. Then, productive cough, anorexia, weight loss, and fatigue are common complaints. Death eventually results from intercurrent infection, cor pulmonale, or carcinoma of the lung. One patient with a typical course was given corticotropin for ten days, with euphoria but no significant objective change. At autopsy, an adenocarcinoma was found originating in the inferior lingual segment of the left upper lobe bronchus. A metastatic tumor was seen in the fourth lumbar vertebra. Asbestosis is associated with bronchogenic carcinoma in 13.8 per cent of the cases cited in the literature. In silicosis, the incidence is considerably less than this. The asbestos particle may serve as a carcinogen because of the chronic mechanical irritation it produces. Since approximately 10,000 workers are engaged in potentially hazardous asbestos operations in this country, it is reasonable to assume that there are many unrecognized cases of asbestosis. A high incidence of bronchogenic carcinoma should be expected in this group.—*Asbestosis and bronchogenic cancer, K. J. Isselbacher, H.*

*Klaus, & H. Hardy, Am. J. Med., November, 1953, 15:* 721.—*(T. H. Noehren)*

**Electric Arc Welding.**—The fumes of welding, particularly those arising from fluorides, cadmium and chromium, are irritating to the mucosa of the respiratory tract. Cough, expectoration, chest pain, sense of oppression about the thorax, and hemoptysis with fever known as "metal fume fever" may develop as an acute reaction. These symptoms subside when exposure to the fumes is avoided. If the exposure is continued, roentgenographic changes in the lungs, such as exaggerated linear shadows in some and nodulation in others, may occur. These are due to deposition of ferrous particles within the perivascular and peribronchial lymphatics. Of 7 cases, 3 showed disabling symptoms due mainly to emphysema and fibrosis. Two patients were not disabled and in 2 tuberculosis developed.—*Respiratory disorders among welders, R. Charr, J.A.M.A., August 15, 1953, 152: 1520.—(H. Abeles)*

**Histoplasmosis in Eastern States.**—Histoplasmosis is commonly considered in the differential diagnosis of pulmonary diseases in endemic areas but is rarely suggested in the eastern United States. Americans travel so freely that many adults in any part of the country have been exposed to *Histoplasma capsulatum*. Pulmonary lesions in adults residing in any part of the United States may have been caused by infection with *H. capsulatum* in an endemic area, without associated symptoms. Months or years later these lesions may be detected in routine chest roentgenograms and become diagnostic problems. Tuberculosis usually is first considered, but their appearance can suggest mediastinal tumors or pulmonary neoplasms. Failure to consider pulmonary histoplasmosis in non-endemic regions will lead to diagnostic errors. In eighteen months at the Pulmonary Clinic of the Veterans Administration Regional Office, Brooklyn, New York, 19 patients with pulmonary lesions had positive histoplasmin skin tests and negative tuberculin and coccidioidin tests. Another 18 patients with similar chest roentgenograms had positive histoplasmin and tuberculin skin tests and negative coccidioidin tests.—*Histoplasmin in non-endemic regions, L. J. Spitz & B. Schwartz, Am. J. Med., December, 1953, 15: 624.—(T. H. Noehren)*

**Heart Disease Detection.**—Among 682 persons having chest microfilms and subsequent clinical investigations, 56 had clinical evidence of heart disease. Only 25 (45 per cent of the 56 with heart disease were noted as having abnormal hearts on the microfilms. There were, in addition, 12 persons who were thought to have abnormal cardiac silhouettes on the microfilms but who did not prove to have heart disease on clinical study. Because of its low degree of detection, the microfilm is not recommended for use in large surveys for finding persons with heart disease (Author's summary).—*Heart disease discovered on chest microfilms, R. V. Slattery, J.A.M.A., August 22, 1953, 152: 1595.—(H. Abeles)*